NEW TANDEM REACTIONS INVOLVING

NUCLEOPHILIC AROMATIC SUBSTITUTION

By

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CHAPTER I

REVIEW OF TANDEM S_NAr REACTIONS

Introduction

Tandem reactions are processes that involve the sequential occurrence of multiple organic reactions in a single laboratory operation. This advantage allows tandem reactions to diminish the operating cost and reduce the waste produced in an organic synthesis by minimizing the amount of solvents and reagents consumed as well as the number of purifications performed a synthesis. Many tandem reactions offer the advantage of forming several bonds through a high atom economy sequence to generate complex molecules.[1] With the public's growing concern over environmental issues and a fear that chemistry could negatively influence the ecological balance, scientists must not only be focused on what to synthesize, but how it is synthesized. By minimizing the amount of side products, solvent consumption and decrease in the number of synthetic steps, tandem reactions can provide economic and ecological benefits when employed in an organic synthesis.

Tandem reactions have been reported extensively in the synthetic chemistry literature.[2] Tandem reactions have been divided into several groups based on the first step of the mechanism in the reaction. These groups have included anionic, radical, pericyclic, photochemical and transition metal induced processes. Furthermore, new

methods are being reported which have included Suzuki cross couplings[3] and microwave assisted reactions.[4] Until recently, nucleophilic aromatic substitution (S_NAr) reactions have been sparsely utilized in tandem processes.

The S_NAr reaction can provide a convenient method for addition of heteroatom and carbon groups onto aromatic rings during a tandem reaction. This is accomplished through displacement of an activated aromatic halide by nucleophiles such as amines, alcohols and carbanions. These nucleophiles can come from the initial reagent used to start the tandem reaction or as an intermediate during the tandem process. There are relatively few literature examples of S_NAr reactions being used in a tandem sequence. The following section gives a representative sampling of the transformations that have been reported.

Tandem S_NAr Amination-Reduction Reaction

Singaram and co-workers[5] developed a novel tandem S_NAr amintation-reduction reaction through the use of lithium *N,N*-dialkylaminoborohydride (LAB) reagents. When 2-halobenzonitriles **1** were treated with various alkyl substituted LAB reagents, it resulted in the formation of the corresponding 2-(*N,N*-dialkylamino)benzylamines **3**. In this reaction the LAB reagents first act as a nucleophile, resulting in a S_NAr reaction, followed by the evolution of BH_3 and the lithium halide salt. The BH_3 then reduces the aryl substituted nitrile to the benzylamine functional group. The authors studied the effects of differing the halide with the use of *N,N*-dimethylaminoborohydride (**2**) as the LAB reagent. It was found that the 2-chloro and 2-fluorobenzonitriles gave primarily the tandem products **3**, but when the compound contained a bromine, the reaction gave

mainly the nitrile-reduction product, 2-bromobenzylamine (**4**). These observations were also seen for other alkyl substituted LAB reagents during the study.

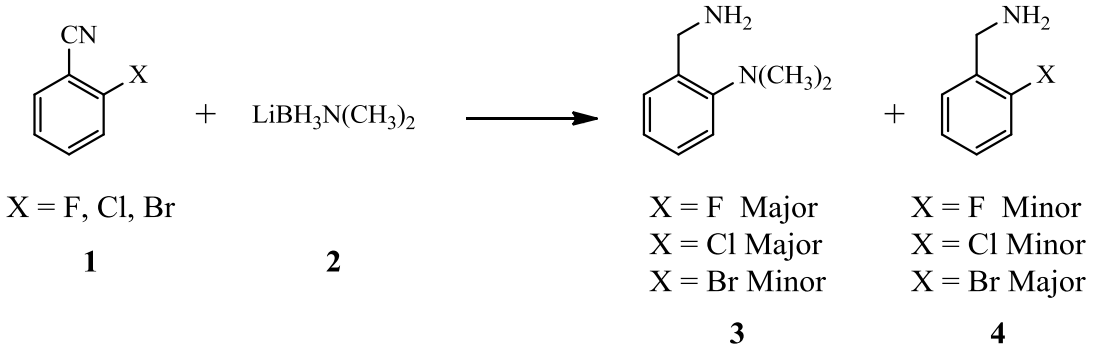
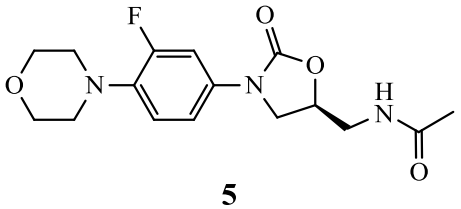


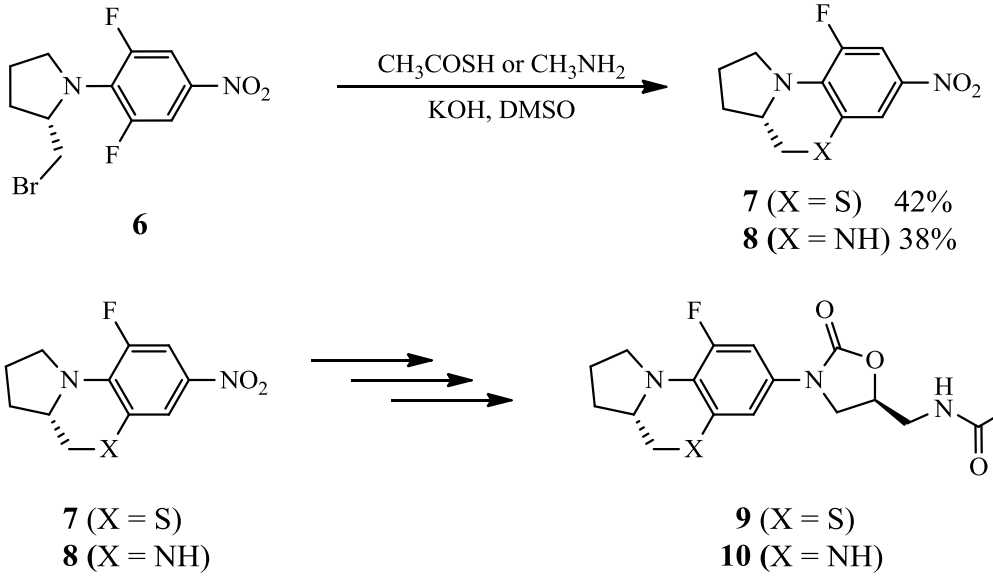
Figure 1. Benzylamines by a tandem S_NAr amination-reduction.

Synthesis of Tricyclic Substituted Oxazolidinones

A class of tricyclic substituted oxazolidinones, which are similar in structure to the synthetic antibiotic linezolid (**5**),[6] have been studied for their antibacterial properties. These have included activities against Gram-positive bacteria and vancomycin-resistant enterococci.[6] Selvakumar and co-workers[7] utilized a tandem S_N2-S_NAr reaction in an approach to synthesize second generation, conformationally constrained, sulfur- and nitrogen-containing analogs of linezolid. Using an aromatic substituted *L*-prolinol derivative **6** the authors were able to react either thioacetic acid/KOH or H_2NMe to give the corresponding tricyclic tandem products **7** and **8**, respectively. The nitro group was then utilized in the production of the oxazolidinone ring to give the desired conformationally constrained analogs of linezolid **9** and **10**.



5
Linezolid



6

7 (X = S) 42%
8 (X = NH) 38%

7 (X = S)
8 (X = NH)

9 (X = S)
10 (X = NH)

Figure 2. Synthesis of linezolid analogs by a tandem S_N2-S_NAr reaction.

Synthesis of Functionalized Carbazoles

The carbazole ring system has been shown to exhibit many biological activities.[8] Both synthetic and naturally occurring carbazole derivatives have presented antimicrobial/anti-inflammatory properties and an ability to inhibit the CDK-5 enzyme. Jean and co-workers[3] were able to develop a tandem cross coupling-S_NAr reaction that utilized a Suzuki type reaction to make functionalized carbazole ring systems. By using aniline-derived boronic esters **11** and a variety of substituted dihalobenzenes **12**, a microwave-assisted, palladium-catalyzed Suzuki reaction provided diaryl intermediates. These intermediates then underwent an intramolecular S_NAr reaction to produce

functionalized carbazoles **13** in modest to excellent yields. *N*-Methylsulfonyl anilines and dihalobenzenes bearing electron-withdrawing groups were essential for the S_NAr portion of the tandem reaction.

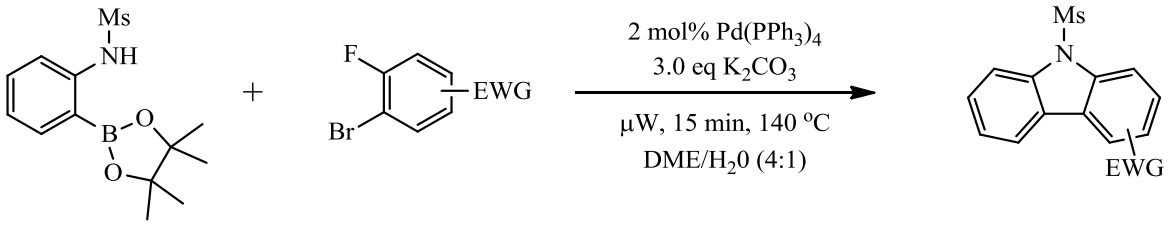


Figure 3. Synthesis of functionalized carbazoles by a tandem cross coupling-S_NAr reaction.

Synthesis of Unsymmetrical Diphenyl Ethers

Xu and co-workers[9] developed an environmentally green, K_2CO_3-mediated tandem deprotection-S_NAr appoarch to the synthesis of unsymmetrical diphenyl ethers by using an ionic liquid, 1-butyl-3-methylimidazolium tetrafluoroborate ([Bmim]BF_4), as the solvent for the reaction. The authors were able to recover and reuse this solvent for subsequent reactions without loss of efficacy. The tandem reaction was initiated by deprotection of a phenyl methanesulfonate **14** using anhydrous K_2CO_3. Subsequently, the newly formed phenol underwent a S_NAr reaction in the presence of an activated fluorobenzene **15** to give the substituted diphenyl ether **16**. Using this method the authors were able to make a large number of unsymmetrically substituted diphenyl ethers in moderate to good yields. However, the reaction had to be run at high temperatures and the substituents were limited to electron withdrawing groups.

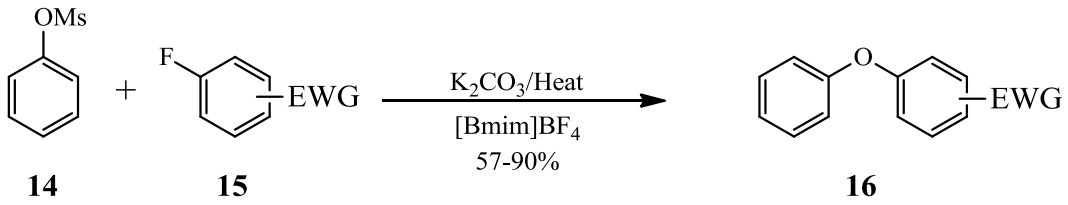


Figure 4. Synthesis of unsymmetrical diphenyl ethers by a tandem deprotection-S_NAr reaction.

Synthesis of 3,6-disubstituted-1*H*-pyrazolo[3,4-*b*]pyridines

Zhong and co-workers[10] were able to prepare various 3,6-disubstituted-1*H*-pyrazolo[3,4-*b*]pyridines **20** *via* a tandem sequence involving a S_NAr reaction followed by a hydrazine initiated S_NAr-pyrazole formation. The synthesis began by preparation of tandem precursors, 2,6-difluoro-3-ketopyridines **19**. This was accomplished by deprotonation of 2,6-difluoropyridine **17** using *n*-butyllithium at -60 ^oC, followed by quenching with a variety of Weinreb amides **18**. A series of 3,6-disubstituted-1*H*-pyrazolo[3,4-*b*]pyridines **20** were then prepared from the 2,6-difluoro-3-ketopyridines in moderate to good yields. The tandem reaction sequence begins by a selective nucleophilic substitution of the 6-fluoride in *N*,*N*-dimethylacetamide (DMA). This is followed by hydrazine substitution of the 2-fluoride and pyrazole formation. These transformations all occurred in a one-pot operation using very mild conditions (0 ^{o} to 25 ^oC). A variety of nitrogen-, oxygen- and sulfur-containing nucleophiles were utilized in the initial nucleophilic substitution of the 6-fluoro to expand the number of potential compounds possible by this tandem reaction sequence.

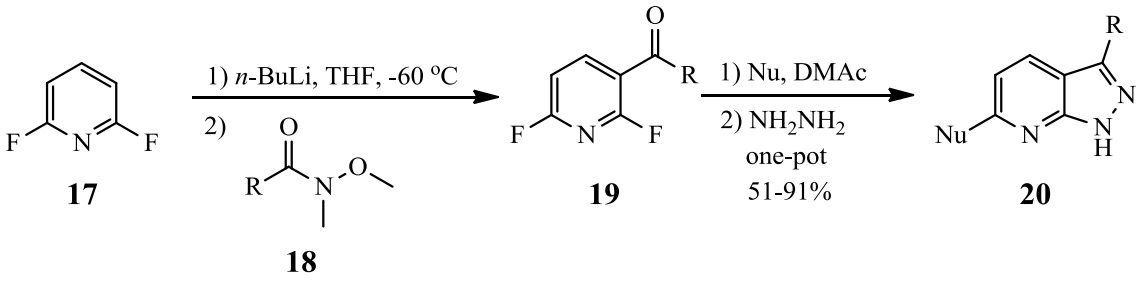
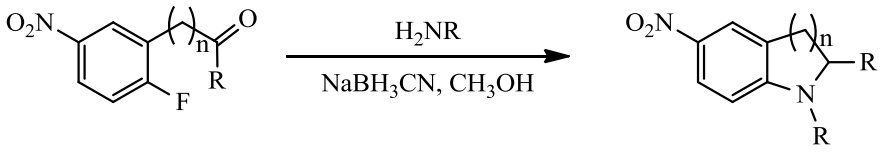


Figure 5. Synthesis of 3,6-disubstituted-1*H*-pyrazolo[3,4-*b*]pyridines.

Tandem Reductive Amination-S_NAr Reaction

Recently Bunce and Nago developed a set of conditions that would generate 5-nitro-2,3-dihydro-1*H*-indoles through a tandem reductive amination-S_NAr reaction.[11] Using this methodology the authors were also able to synthesize 6-nitro-1,2,3,4-tetrahydroquinolines.[12] Both reports used easily synthesized fluorobenzene derivatives bearing appropriately placed carbonyl side chains **21** and **22**. The addition of a primary amine and sodium cyanoborohydride initiated a reductive amination reaction. The amine containing intermediates then underwent a intramolecular S_NAr reaction. The authors were able to generate a series of 5-nitro-2,3-dihydro-1*H*-indoles products **23** when n =1 and, a series of 1-alkyl-6-nitro-1,2,3,4-tetrahydroquinolines **24** when n = 2.



21 (n = 1)
22 (n = 2)

23 (n = 1)
24 (n = 2)

Figure 6. Synthesis of 2,3-dihydro-1*H*-indoles and 1,2,3,4-tetrahydroquinolines.

In both cases, it was found that branching at the α–carbon of the primary amines greatly reduced the yields of the final tandem products. This was believed to be caused by an increase in steric hindrance of the incoming amine. This steric hindrance led to the

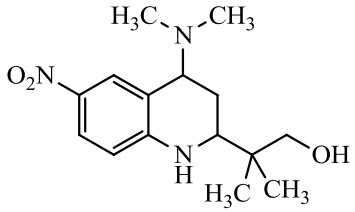
isolation of uncyclized compounds in the cases of cyclohexyl- and *tert*-butylamines which were unable to complete the tandem reaction to form the corresponding heterocycle products.

CHAPTER II

6-NITRO-1,2,3,4-TETRAHYDROQUINOLINE-4-CARBOXYLIC ESTERS AND 7-NITRO-3,4-DIHYDROQUINOXALINE-1(2*H*)-CARBOXYLIC ESTERS BY A TANDEM REDUCTIVE AMINATION-S_NAr REACTION

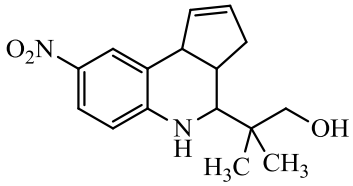
Introduction

Earlier work in our laboratory included the development of a tandem reductive amination-S_NAr reaction to prepare tetrahydroquinolines.[12] It was envisioned that this tandem reaction could be expanded to include ester-substituted 1,2,3,4-tetrahydroquinolines and 3,4-dihydroquinoxalines. Tetrahydroquinolines have shown useful activities in the treatment of inflammatory diseases such as asthma.[13] A recent report has revealed that certain 2-substituted-6-nitro-1,2,3,4-tetrahydroquinolines promote increased bone mineral density in rats and thus may have potential for the treatment of osteoporosis.[14] These compounds include the SARM candidates[15] S-40503 (**1**), and 2-methyl-2-(8-nitro-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolin-4-yl)propan-1-ol (**2**) that bind to the androgen receptor with nanomolar affinity.



1

S-40503

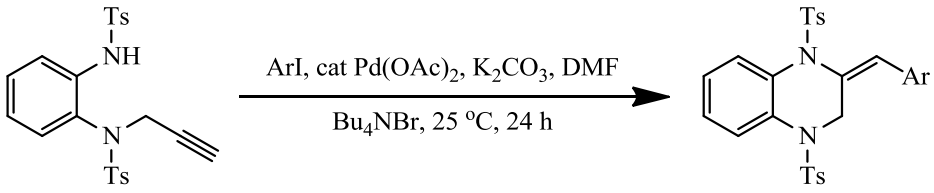


2

2-methyl-2-(8-nitro-3a,4,5,9b-tetrahydro-3*H*-cyclopenta[*c*]quinolin-4-yl)propan-1-ol

Figure 1. Tetrahydroquinoline SARM candidates.

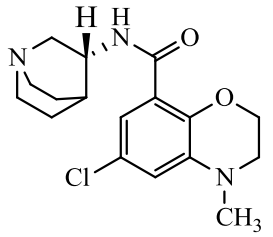
In addition, dihydroquinoxaline derivatives have been shown to express useful activity as anticancer drugs[16] and as cell adhesion agents.[17] Mukhopadhyay showed that (*E*)-tetrahydroquinoxaline **4** could be formed through a regio- and stereoselective palladium-catalyzed heterocyclization of tosylamide **3** with aryl iodides.[18] The cyclization takes place in good yields using $Pd(OAc)_2$ as the catalyst in the presence of Bu_4NBr and K_2CO_3.



3 **4**

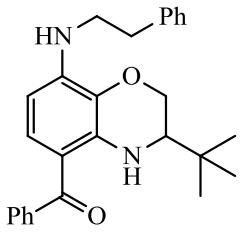
Figure 2. Synthesis of (*E*)-tetrahydroquinoxalines.

The tandem reductive amination-S_NAr reaction may provide a new route to 3,4-dihydrobenzoxazines. Dihydrobenzoxazines have demonstrated activity as antihypertensives with (*S*)-*N*-(1-azabicyclo[2.2.2]oct-3-yl)-6-chloro-3,4-dihydro-4-methyl-2*H*-1,4-benzoxazine-8-carboxamide[19] (**5**) and neuroprotective agents including S24429 (**6**) and S24718 (**7**).[20]



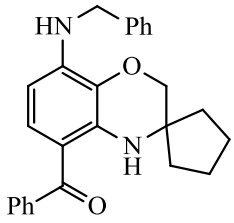
5

(*S*)-*N*-(1-azabicyclo[2.2.2]oct-3-yl)-6-chloro-3,4-dihydro-4-methyl-2*H*-1,4-benzoxazine-8-carboxamide



6

S 24429

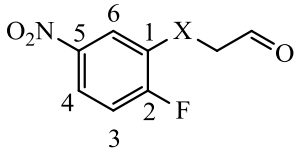


7

S 24718

Figure 3. Biologically active dihydrobenzoxazines.

To synthesize the 1,2,3,4-tetrahydroquinolines, 3,4- dihydroquinoxalines and 3,4-dihydrobenzoxazines with a tandem reductive amination-S_NAr, reaction the substrates required should be trisubstituted aromatic systems, bearing a 3-oxo side-chain at C1, a F (or Cl) at C2 and a NO_2 group at C5 (see Figure 4). This system could then undergo the tandem reaction with a primary amine.



X = CH-CO_2CH_3, N-CO_2CH_3 or O

Figure 4. Needed substrates for tandem reaction.

The electronic nature of the atom linkage at the C1 position was anticipated to be a critical factor for success in the final S_NAr ring closure. While the alkyl side chain of the tetrahydroquinoline precursors should not pose a problem, the alkylamino group in the dihydroquinoxaline precursors and the alkoxy side chain in the dihydrobenzoxazines precursor would deactivate the ring toward the final S_NAr cyclization by creating an electron rich aromatic system. In the dihydroquinoxaline precursors, the electron donating character of the nitrogen could be decreased by altering the side-chain nitrogen as a carbamate. Derivatization, however, would not be possible in the case of the dihydrobenzoxazine precursors, and we anticipated difficulties in the ring closure step using these substrates.

Results

Synthesis of Precursors

The precursors needed for synthesizing the 1,2,3,4-tetrahydroquinolines were prepared from methyl 2-fluoro-5-nitrophenylacetate (**9**) which was available by esterification of 2-(2-fluoro-5-nitrophenyl)acetic acid (**8**).[21] The acidity of the benzylic CH allowed for deprotonation and allylation α to the aromatic ring. Thus, alkylation using 3-iodo-1-propene or 3-iodo-2-methyl-1-propene generated **10** and **11**, respectively. Ozonolysis[22] then converted the side-chain double bonds to the necessary carbonyl containing precursors **12** and **13**, respectively.

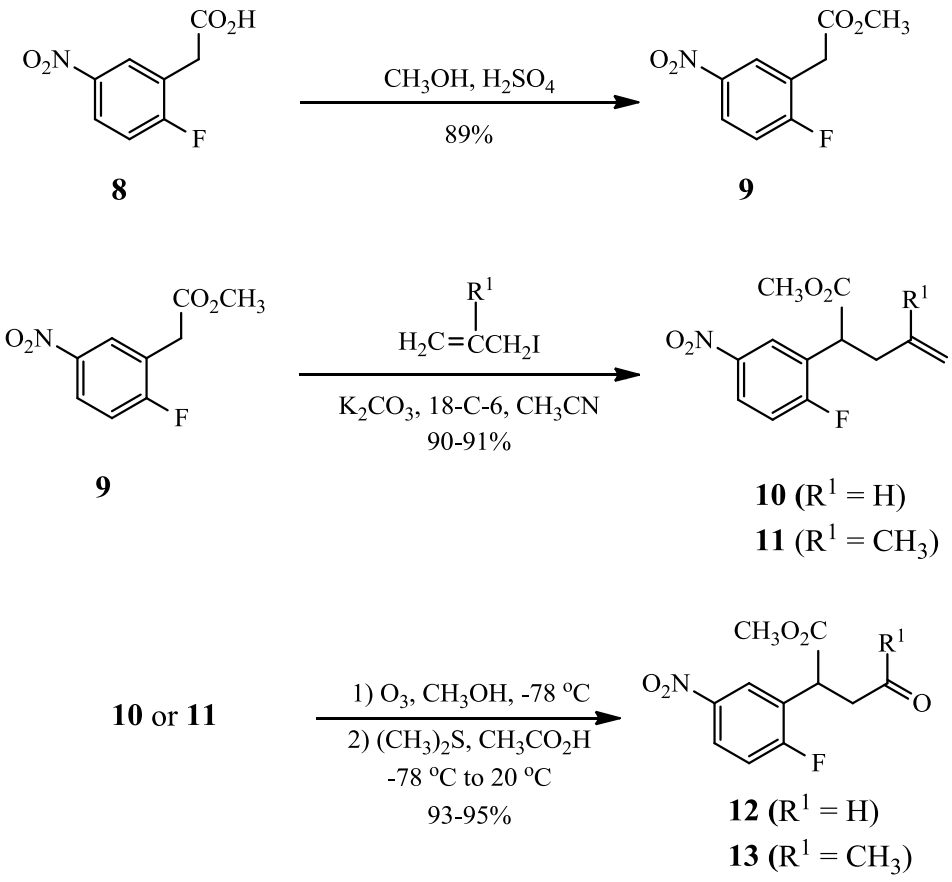


Figure 5. Preparation of the tetrahydroquinoline precursors.

The 3,4- dihydroquinoxaline precursors were generated from 2-fluoro-5-nitroaniline (**14**). First, the amine group of the aromatic ring was converted to a methyl carbamate (**15**) using pyridine and methyl chloroformate. Conversion to the carbamate decreases the electron donating character of the nitrogen that would tend to deactivate the ring toward the final S_NAr cyclization. Deprotonation of the carbamate NH allowed alkylation by 3-iodo-1-propene or 3-iodo-2-methyl-1-propene to generate **16** and **17**, respectively. The side-chain double bonds were then subjected to ozonolysis resulting in the desired nitrogen precursors **18** and **19**.

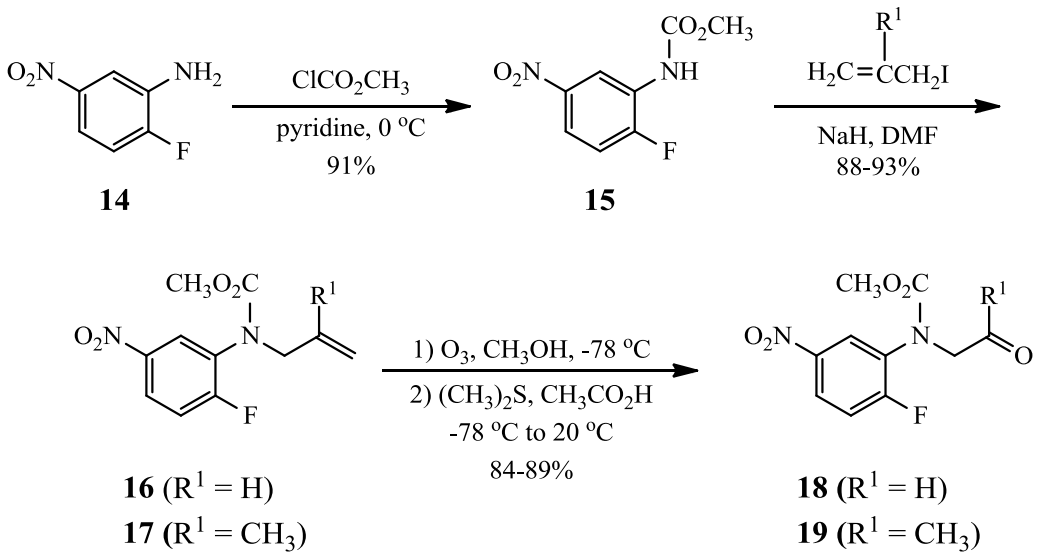


Figure 6. Preparation of the dihydroquinoxaline precursors.

Lastly, a dihydrobenzoxazine precursor was also prepared. Unfortunately the 2-fluoro-5-nitrophenol was not commercially available and attempts to generate it by a Schiemann reaction[23] failed. Thus commercial 2-chloro-5-nitrophenol **20** was used instead.[24] The phenol was deprotonated using K_2CO_3 and alkylated with 3-iodo-2-methyl-1-propene to give **21**. Ozonolysis again converted the side-chain double bond to the necessary ketone precursor **22**.

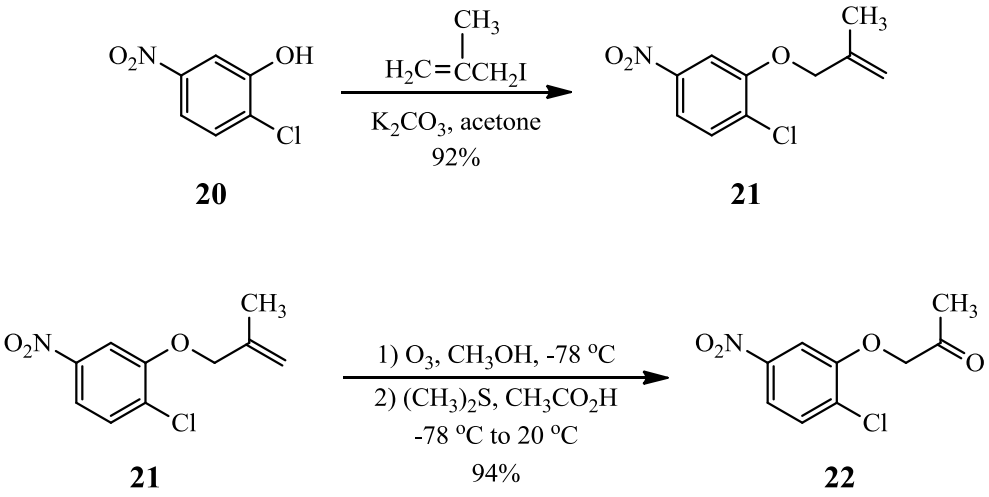
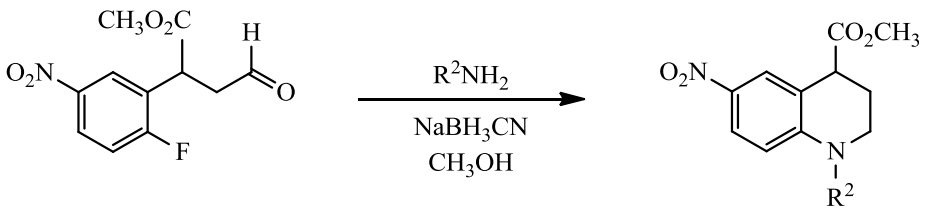


Figure 7. Preparation of the dihydrobenzoxazine precursor.

Conducting the Tandem Reductive Amination-S_NAr Reaction

Once the substrates were available, investigation of the tandem reductive amination-S_NAr reaction was initiated. Beginning with the synthesis of tetrahydroquinolines, the aldehyde precursor **12** was the first substrate to be examined. Reaction conditions were based on the work of Bunce and Nago.[12] The reaction was carried out by dissolving 1.00 eq of the carbonyl compound **12** in CH_3OH and adding 1.20 eq of benzylamine. The solution was stirred for 30 min, followed by addition of a total of 1.40 eq of $NaBH_3CN$ in three approximately equal portions over 30 minutes. The use of excess $NaBH_3CN$ insured that the reductive amination reaction would occur allowing for the subsequent nucleophilic aromatic substitution. The target molecule **23a** was isolated after workup in a yield of 90%. A series of primary amines was then used in the tandem reaction to give products **23b-d**. The results from these reactions are given in Table 1.



12

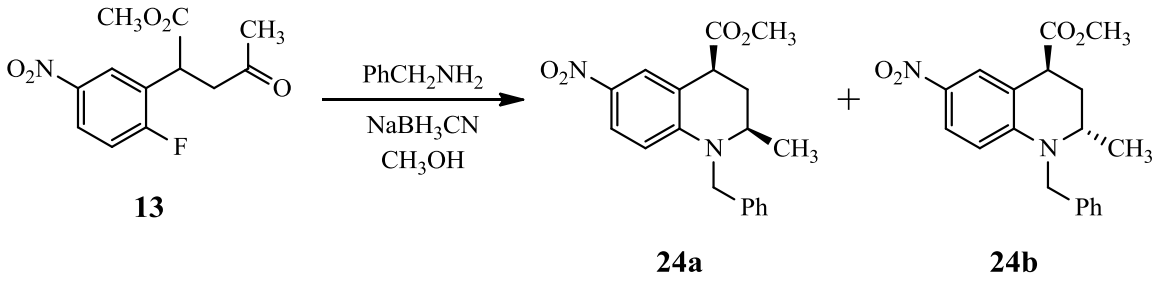
23a ($R^2 = CH_2Ph$)
23b ($R^2 = n\text{-}C_6H_{13}$)
23c ($R^2 = i\text{-}C_4H_9$)
23d ($R^2 = c\text{-}C_6H_{11}$)

Figure 8. Tandem reductive amination-S_NAr reaction to prepare tetrahydroquinolines.

R^2	product	yield (%)
CH_2Ph	**23a**	90
$n\text{-}C_6H_{13}$	**23b**	74
$i\text{-}C_4H_9$	**23c**	89
$c\text{-}C_6H_{11}$	**23d**	70

Table 1. Tandem reductive amination-S_NAr reaction to prepare tetrahydroquinolines.

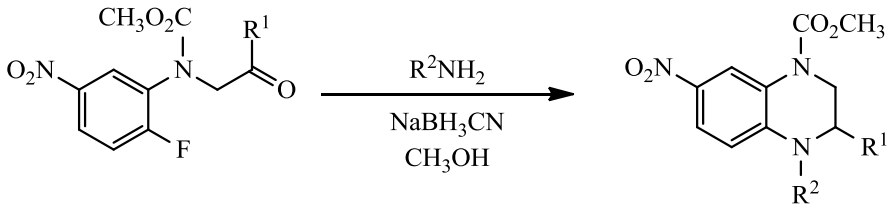
The ketone precursor **13** for the tetrahydroquinolines was reacted in the same manner. Unlike the aldehyde precursor, the ketone precursor introduced an additional stereocenter at the 2 position of the ring in the final product. It was our hope that the product would exhibit a preferred orientation in the formation of the stereocenters. However, the first reaction with benzylamine yielded a mixture of inseparable *cis* and *trans* stereoisomers **24a** and **24b**. Based on this result, further reactions were not pursued with the ketone precursor **13**.



13 **24a** **24b**

Figure 9. Ring closure of ketone precursor.

Continuing to develop the tandem reductive amination-S_NAr reaction, the dihydroquinoxaline precursors **18** and **19** were treated in the same manner with the series of primary amines to give the products **25a-d** and **26a-d**, respectively. In the case of the ketone precursor **19**the lack of stereoselectivity that plagued the tetrahydroquinoline analog was no longer a factor. Reactions with the aldehydes generally gave lower yields than the ketones. This is because the aldehyde precursor **18** generally yielded 5–20% of the simple reductive amination product in addition to the ring-closed product. Adjustment of the reaction conditions and stoichiometry of reagents had little effect on this outcome. In addition, when the R group of the amine was a secondary alkyl group, the yields were diminished in both cases as demonstrated in Table 2.



18 (R^1= H)
19 (R^1= CH_3)

25a (R^1 = H, R^2 = CH_2Ph)
25b (R^1 = H, R^2 = *n*-C_6H_{13})
25c (R^1 = H, R^2 = *i*-C_4H_9)
25d (R^1 = H, R^2 = *c*-C_6H_{11})

26a (R^1 = CH_3, R^2 = CH_2Ph)
26b (R^1 = CH_3, R^2 = *n*-C_6H_{13})
26c (R^1 = CH_3, R^2 = *i*-C_4H_9)
26d (R^1 = CH_3, R^2 = *c*-C_6H_{11})

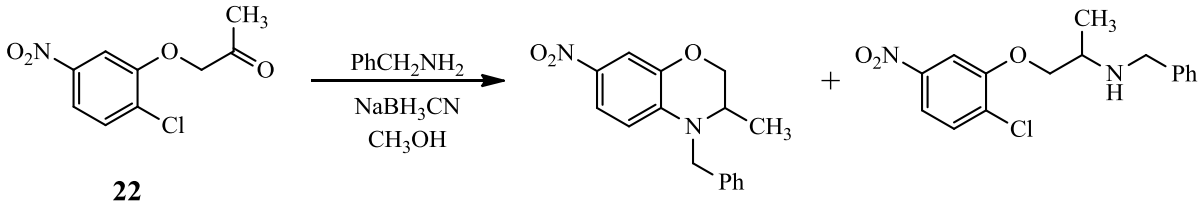
Figure 10. Tandem reductive amination-S_NAr reaction to prepare dihydroquinoxalines.

R^1	R^2	product	yield (%)
H	CH_2Ph	**25a**	52
H	*n*-C_6H_{13}	**25b**	62
H	*i*-C_4H_9	**25c**	55
H	*c*-C_6H_{11}	**25d**	36
CH_3	CH_2Ph	**26a**	83
CH_3	*n*-C_6H_{13}	**26b**	69
CH_3	*i*-C_4H_9	**26c**	75
CH_3	*c*-C_6H_{11}	**26d**	57

Table 2. Tandem reductive amination-S_NAr reaction to prepare tetrahydroquinoxalines.

Finally, an attempt to close a dihydrobenzoxazine ring using the oxygen-containing precursor **22** with benzylamine was made. From this substrate, we observed only the simple reductive amination product **28** (46%), along with recovered starting

material (28%); none of the desired product **27** was formed. In an attempt to facilitate closure of the simple reductive amination product **28**, the reaction was rerun at 50 ^{o}C. However, none of the ring-closed product was formed from the reaction. This is presumably due to the unfavorable electronics created by the electron donating ether group on the aromatic ring. Unfortunately the less reactive chlorine group could not be replaced with the more electronegative fluorine group as the fluoronitroaromatic substrate was not commercially available and could not be prepared by the Schiemann reaction.[23]



22 **27** not observed **28** (46%)

Figure 11. Attempted synthesis of dihydrobenzoxazine.

Conclusion

A tandem reductive amination-S_NAr reaction was developed to synthesize 1,2,3,4-tetrahydroquinolines bearing an ester functional group at the 4 position. The nitrogen analogs, 3,4-dihydroquinoxalines, bearing carbamate protection at N1, has also been prepared. However, the oxygen-containing 3,4-dihydrobenzoxazines were not available by this method. It is, thus, essential for the reactants to contain an electron deficient aromatic system bearing a donating group in order for the S_NAr reaction to occur. In the case where electron deficiency was not possible, the reaction failed to close the heterocyle in the final step.

The reaction is also sensitive to steric hindrance in the amine. When the amine had an alkyl group branched α to the amine N, the reaction yields were reduced. Though the current approach to the tetrahydroquinoline systems is not as diastereoselective as the earlier-reported reduction-reductive amination,[22] it does offer a relatively direct route to the title compounds.

Experimental Section

All reactions were run in dry glassware under N_2. The saturated NH_4Cl, saturated NaCl, 5% $NaHCO_3$, 5% $Na_2S_2O_3$ and 0.5 M HCl, used in work-up procedures refer to aqueous solutions. Reactions were monitored by TLC on silica gel GF plates (Analtech 21521).

Preparative separations were performed by one of the following methods: (1) flash column chromatography on silica gel (grade 62, 60–200 mesh) containing UV-active phosphor (Sorbent Technologies UV-05) packed into quartz columns or (2) PTLC on 20-cm × 20-cm silica gel GF plates (Analtech No 02015). Band elution for all chromatographic separations was monitored using a hand-held UV lamp. Melting points were uncorrected. IR spectra were run as thin films on NaCl disks. ^{1}H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ at 300 MHz and 75 MHz, respectively, using $Si(CH_3)_4$ as the internal standard; coupling constants (*J*) are given in Hz. Mass spectra (EI/DP) were obtained at 70 eV.

Methyl 2-Fluoro-5-nitrophenylacetate (9).

A solution of 2-fluoro-5-nitrophenylacetic acid (**8**)[25] (5.00 g, 25.1 mmol) in CH_3OH (100 mL) containing 2 mL of concentrated H_2SO_4 was refluxed for 24 h, and then cooled, concentrated, poured into ice water and extracted with ether (3x). The combined ether extracts were washed with 5% $NaHCO_3$ (2x) and saturated NaCl (1x), then dried ($MgSO_4$) and concentrated under vacuum to give the ester as a light yellow oil that slowly crystallized. The crude solid was triturated with 1% ether in pentane and filtered

to give **9** (4.74 g, 89%) as a light yellow solid; mp 52–55 ^{o}C: IR: 1743, 1529, 1350, 1250 cm^{-1}; ^{1}H NMR: δ 8.22 (m, 2 H), 7.23 (t, *J* = 8.8 Hz, 1 H), 3.77 (d, *J* = 1.1 Hz, 2 H), 3.75 (s, 3 H); ^{13}C NMR: δ 169.7, 164.6 (d, *J* = 257.9 Hz), 144.1, 127.5 (d, *J* = 6.1 Hz), 125.1 (d, *J* = 10.7 Hz), 123.1 (d, *J* = 18.3 Hz), 116.4 (d, *J* = 24.4 Hz), 52.5 (d, *J* = 3.8 Hz), 34.0 (d, *J* = 2.3 Hz); MS: *m/z* 213 (M^{+}).

Anal. Calcd for $C_9H_8FNO_4$: C, 50.70; H, 3.76; N, 6.57. Found: C, 50.73; H, 3.77; N, 6.53.

Methyl N-(2-Fluoro-5-nitrophenyl)carbamate (15).

To a stirred solution of 2-fluoro-5-nitroaniline (**14**) (5.00 g, 32.0 mmol) in pyridine (50 mL)at 0 ^{o}C was slowly added methyl chloroformate (3.35 g, 2.74 mL, 35.4 mmol) over 30 min. The reaction was stirred for 2 h with gradual warming to 22 ^{o}C. The crude reaction mixture was added to water and ether extracted (3x). The combined ether extracts were washed with 0.5 *M* HCl (4x), water (1x) and NaCl (1x) and then dried ($MgSO_4$) and concentrated under vacuum to give a brown powder. Trituration of this solid with ether gave **15** (5.75 g, 91%) as tan crystals; mp 116–118 ^{o}C (lit[26] mp 116–118 ^{o}C). IR: 3401, 1740, 1533, 1348, 1245 cm^{-1}; ^{1}H NMR: δ 9.08 (br d, *J* = 4.8 Hz, 1 H), 7.94 (ddd, *J* = 9.1, 4.2, 2.7 Hz, 1 H), 7.23 (t, *J* = 9.1 Hz, 1 H), 7.02 (br s, 1 H), 3.86 (s, 3 H); ^{13}C NMR: δ 154.9 (d, *J* = 254.1 Hz), 153.1, 144.7, 127.5 (d, *J* = 11.4 Hz), 118.9 (d, *J* = 9.2 Hz), 115.6 (d, *J* = 3.4 Hz), 115.4 (d, *J* = 22.1 Hz); MS: *m/z* 214 (M^{+}).

Anal. Calcd for $C_8H_7FN_2O_4$: C, 44.86; H, 3.27; N, 13.08. Found: C, 44.77; H, 3.31; H, 13.16.

Representative Alkylation Procedure for the Ester: Methyl 2-(2-Fluoro-5-nitrophenyl)-4-pentenoate (10).

The general procedure of Makosza and Tyrala was followed.[27] In a 100-mL, three-necked, round-bottomed flask, a solution of **9** (1.07 g, 5.00 mmol) in dry CH_3CN (10 mL) was added to a suspension of anhydrous K_2CO_3 (5.80 g, 42.0 mmol) and 18-crown-6 (10 mg) in dry CH_3CN (40 mL). To the resulting red mixture was added 1.01 g (0.55 mL, 6.00 mmol) of 3-iodo-1-propene. The reaction was stirred under reflux for 6 h and then cooled to 22 ^oC and filtered to remove the solids. The solids were washed with ether and the filtrate was concentrated under vacuum. The remaining oil was purified by flash chromatography on a 30 cm × 2 cm silica gel column eluted with 5–10% ether in hexanes to give **10** (1.15 g, 91%) as a light yellow oil. IR: 1738, 1646, 1529, 1350, 1245 cm^{-1}; ^1H NMR: δ 8.30 (dd, *J* = 6.2, 2.7 Hz, 1 H), 8.18 (ddd, *J* = 9.0, 4.4, 2.7 Hz, 1 H), 7.21 (t, *J* = 9.0 Hz, 1 H), 5.70 (ddt, *J* = 17.0, 10.2, 7.0 Hz, 1 H), 5.05 (m, 2 H), 4.07 (t, *J* = 7.1 Hz, 1 H), 3.72 (s, 3 H), 2.90 (m, 1 H), 2.59 (m, 1 H); ^{13}C NMR: δ 171.9, 164.0 (d, *J* = 257.9 Hz), 144.4, 133.7, 127.4 (d, *J* = 9.0 Hz), 125.6 (d, *J* = 6.1 Hz), 124.8 (d, *J* = 9.9 Hz), 118.2, 116.5 (d, *J* = 25.1 Hz), 52.5, 43.5, 36.3; MS: *m/z* 253 (M^+).

Anal. Calcd for $C_{12}H_{12}FNO_4$: C, 56.92; H, 4.74; N, 5.53. Found: C, 56.99; H, 4.77; N, 5.49.

Methyl 2-(2-Fluoro-5-nitrophenyl)-4-methyl-4-pentenoate (11).

Ester **11** (1.20 g, 90%) was prepared as above from **9** (1.07 g, 5.00 mmol) and 3-iodo-2-methyl-1-propene (1.09 g, 6.00 mmol) isolated asa light yellow oil. IR: 1738, 1651, 1533,

1350, 1248 cm^{-1}; ^{1}H NMR: δ 8.32 (dd, *J* = 6.2, 2.7 Hz, 1 H), 8.18 (m, 1 H), 7.21 (t, *J* = 9.0 Hz, 1 H), 4.74 (s, 1 H), 4.64 (s, 1 H), 4.23 (t, *J* = 7.7 Hz, 1 H), 3.71 (s, 3 H), 2.88 (dd, *J* = 14.4, 7.3 Hz, 1 H), 2.54 (dd, *J* = 14.4, 8.4 Hz, 1 H), 1.74 (s, 3 H); ^{13}C NMR: δ 172.2, 164.0 (d, *J* = 257.1 Hz), 144.3, 141.1, 127.5 (d, *J* = 16.8 Hz), 125.5 (d, *J* = 6.1 Hz), 124.6 (d, *J* = 9.9 Hz), 116.4 (d, *J* = 25.9 Hz), 113.5, 52.5, 42.0, 40.3, 22.0; MS: *m/z* 267 (M^{+}).

Anal. Calcd for $C_{13}H_{14}FNO_4$: C, 58.42; H, 5.24; N, 5.24. Found: C, 58.49; H, 5.26; N, 5.18.

Representative Alkylation Procedure for the Amide: Methyl *N*-(2-Fluoro-5-nitrophenyl)-*N*-(2-propenyl)carbamate (16).

In a 50-mL, three-necked, round-bottomed flask was placed 60% NaH in mineral oil (0.24 g , 6.00 mmol) which was washed with hexanes (3x) and suspended in dry DMF (15 mL). To the stirred suspension at 22 ^{o}C was slowly added a solution of **15** (1.07 g, 5.00 mmol) in dry DMF (5 mL). Stirring was continued for 30 min and a solution of 3-iodo-1-propene (1.01 g, 0.55 mL, 6.00 mmol) in dry DMF (1 mL) was added. The reaction was stirred for 8 h at 22 ^{o}C, quenched with saturated NH_4Cl and extracted with ether (3x). The combined ether extracts were washed with 5% $Na_2S_2O_3$ (1x) and saturated NaCl (1x) and then dried ($MgSO_4$) and concentrated under vacuum. The crude yellow oil **16** (1.19 g, 93%) was spectroscopically pure and was used directly in the next reaction. IR: 1718, 1643, 1528, 1348, 1255 cm^{-1}; ^{1}H NMR: δ 8.20 (m, 2 H), 7.28 (t, *J* = 8.9 Hz, 1 H), 5.86 (ddt, *J* = 17.4, 10.8, 6.0 Hz, 1 H), 5.17 (s, 1 H), 5.13 (dd, *J* = 7.3, 1.3 Hz, 1 H), 4.28 (d, *J* = 6.1 Hz, 2 H), 3.74 (br s, 3 H); ^{13}C NMR: δ 161.2 (d, *J* = 261.1 Hz), 155.0,

144.1, 132.4, 130.2, 125.7 (d, J = 2.9 Hz), 124.4 (d, J = 9.7 Hz), 118.7, 117.1 (d, J = 23.2 Hz), 53.5, 52.7; MS: *m/z* 254 (M^+).

Anal. Calcd for $C_{11}H_{11}FN_2O_4$: C, 51.97; H, 4.36; N, 11.02. Found: C, 51.89; H, 4.39; N, 11.18.

Methyl *N*-(2-Fluoro-5-nitrophenyl)-*N*-(2-methyl-2-propenyl)carbamate (17).

Ester **17** (1.18 g, 88%) was prepared as above from **15** (1.07 g, 5.00 mmol) and 3-iodo-2-methyl-1-propene (1.09 g, 6.00 mmol) isolated asa yellow oil. IR: 1723, 1659, 1533, 1348, 1256 cm^{-1}; ^{1}H NMR: δ 8.18 (m, 2 H), 7.27 (t, J = 9.0 Hz, 1 H), 4.85 (s, 1 H), 4.78 (s, 1 H), 4.26 (s, 2 H), 3.74 (br s, 3 H), 1.77 (s, 3 H); ^{13}C NMR: δ 162.0 (d, J = 261.0 Hz), 155.2, 144.1, 140.1, 130.1, 125.1 (d, J = 2.9 Hz), 124.2 (d, J = 10.0 Hz), 117.1 (d, J = 23.5 Hz), 114.0, 55.7, 53.5, 19.9; MS: *m/z* 268 (M^+).

Anal. Calcd for $C_{12}H_{13}FN_2O_4$: C, 53.69; H, 4.89; N, 10.44. Found: C, 53.58; H, 4.86; N, 10.52.

1-Chloro-2-(2-methyl-2-propenyloxy)-4-nitrobenzene (21).

To a 100-mL, three-necked, round-bottomed flask, a solution of 2- chloro-5-nitrophenol (**20**)[24](0.87 g, 5.00 mmol) in 10 mL of dry acetone was added to a suspension of anhydrous K_2CO_3 (5.80 g, 42.0 mmol) in dry acetone (25 mL). To the resulting mixture was added 3-iodo-2-methyl-1-propene (1.09 g, 6.00 mmol). The reaction was stirred under reflux for 6 h, then cooled to 22 ^{o}C and filtered to remove the solids. The solids

were washed with ether and the filtrate was concentrated under vacuum. The remaining oil was purified by flash chromatography on a 30 cm × 2 cm silica gel column eluted with 5–10% ether in hexanes to give **21** (0.98 g, 92%) as a light yellow oil that solidified on standing; mp 59–60 ^{o}C. IR: 1652, 1528, 1353 cm^{-1}; ^{1}H NMR: δ 7.80 (dd, *J* = 8.5, 2.4 Hz, 1 H), 7.77 (d, *J* = 2.4 Hz, 1 H), 7.52 (d, *J* = 8.5 Hz, 1 H), 5.19 (dd, *J* = 1.3, 0.9 Hz, 1 H), 5.07 (dd, *J* = 2.6, 1.6 Hz, 1 H), 4.61 (s, 2 H), 1.87 (s, 3 H); ^{13}C NMR: δ 154.4, 147.1, 139.0, 130.4, 116.3, 113.94, 113.93, 108.1, 73.0, 19.2; MS: *m/z* 227, 229 (*ca* 3:1, M^{+})

Anal. Calcd for $C_{10}H_{10}ClNO_3$: C, 52.75; H, 4.40; N, 6.15. Found: C, 52.81; H, 4.44; N 6.11.

Representative Ozonolysis Procedure: Methyl 2-(2-Fluoro-5-nitrophenyl)-4-oxobutanoate (12).

The general procedure of Bunce and co-workers was adapted.[22] In a 250-mL, round-bottomed flask, a solution of **10** (1.00 g, 3.95 mmol) in CH_3OH (100 mL) was ozonized at –78 ^{o}C until TLC indicated complete consumption of the starting material. Excess ozone was purged with a stream of dry N_2, and dimethyl sulfide (5.00 g, 5.91 mL, 80.6 mmol) was added. The mixture was warmed to 0 ^{o}C, and acetic acid (5 mL) was added. The solution was stirred at 0 ^{o}C for 1 h and then warmed to 22 ^{o}C and stirred for 8 h. The reaction was concentrated, diluted with ether, washed with 5% $NaHCO_3$ (3x) and saturated NaCl (1x) and then dried ($MgSO_4$). Removal of the ether gave **12** (0.94 g, 93%) as a light yellow oil that solidified on standing; mp 63–64 ^{o}C. The crude product was spectroscopically pure and was used directly in the next reaction. IR: 2842, 2731, 1738,

1724, 1530, 1350, 1249 cm^{-1}; ^{1}H NMR: δ 9.08 (s, 1 H), 8.21 (m, 2 H), 7.25 (t, *J* = 9.0 Hz, 1 H), 4.54 (dd, *J* = 8.4, 5.7 Hz, 1 H), 3.73 (s, 3 H), 3.48 (dd, *J* = 18.8, 8.4 Hz, 1 H), 2.91 (dd, *J* = 18.8, 5.7 Hz, 1 H); ^{13}C NMR: δ 198.0, 171.3, 163.8 (d, *J* = 257.9 Hz), 144.4, 127.0 (d, *J* = 16.8 Hz), 125.6 (d, *J* = 6.1 Hz). 125.3 (d, *J* = 9.9 Hz), 116.9 (d, *J* = 24.4 Hz), 52.9, 45.3, 38.2; MS: *m/z* 255 (M^{+}).

Anal. Calcd for $C_{11}H_{10}FNO_5$: C, 51.76; H, 3.92; N, 5.49. Found: C, 51.81; H, 3.93; N, 5.45.

Methyl 2-(2-Fluoro-5-nitrophenyl)-4-oxopentanoate (13).

Ester **13** (0.96 g, 95%) was prepared as above from **11** (1.00 g, 3.75 mmol) isolated asa yellow oil. IR: 1738, 1717, 1533, 1350, 1250 cm^{-1}; ^{1}H NMR: δ 8.19 (m, 2 H), 7.23 (t, *J* = 9.0 Hz, 1 H), 4.51 (dd, *J* = 8.8, 5.3 Hz, 1 H), 3.71 (s, 3 H), 3.45 (dd, *J* = 18.8, 8.8 Hz, 1 H), 2.80 (dd, *J* = 18.8, 5.3 Hz, 1 H), 2.22 (s, 3 H); ^{13}C NMR: δ 204.7, 171.7, 163.9 (d, *J* = 258.6 Hz), 144.6, 127.4 (d, *J* = 17.5 Hz), 125.6 (d, *J* = 5.3 Hz), 125.1 (d, *J* = 9.9 Hz), 116.7 (d, *J* = 24.4 Hz), 52.8, 45.1, 39.5, 29.8; MS: *m/z* 269 (M^{+}).

Anal. Calcd for $C_{12}H_{12}FNO_5$: C, 53.53; H, 4.46; N, 5.20. Found: C, 53.61; H, 4.44; N, 5.11.

Methyl *N*-(2-Fluoro-5-nitrophenyl)-*N*-(2-oxoethyl)carbamate (18).

Ester **18** (0.85 g, 84%) was prepared as above from **16** (1.00 g, 3.95 mmol) isolated asa yellow oil. IR: 1713, 1533, 1352, 1256 cm^{-1}; ^{1}H NMR: δ 9.70 (s, 1 H), 8.31 (br s, 1 H),

8.21 (m, 1 H), 7.33 (t, *J* = 9.1 Hz, 1 H), 4.45 (s, 2 H), 3.76 (br s, 3 H); ^{13}C NMR: δ 196.2, 161.4 (d, *J* = 260.8 Hz), 155.0, 144.0, 130.1, 125.7, 124.6 (d, *J* = 8.9 Hz), 117.1 (d, *J* = 23.2 Hz), 59.1, 53.9; MS: *m/z* 256 (M^+).

Anal. Calcd for $C_{10}H_9FN_2O_5$: C, 46.88; H, 3.54; N, 10.93. Found: C, 47.02; H, 3.59; N, 10.82.

Methyl *N*-(2-Fluoro-5-nitrophenyl)-*N*-(2-oxopropyl)carbamate (19).

Ester **19** (0.90 g, 89%) was prepared as above from **17** (1.00 g, 3.73 mmol) isolated asa yellow solid; mp 98–100 ^{o}C. IR: 1718, 1533, 1348, 1256 cm^{-1}; ^{1}H NMR: δ 8.37 (br s, 1 H), 8.18 (ddd, *J* = 9.2, 4.1, 3.2 Hz, 1 H), 7.28 (t, *J* = 9.2 Hz, 1 H), 4.43 (s, 2 H), 3.73 (br s, 3 H), 2.20 (s, 3 H); ^{13}C NMR: δ 202.0, 161.5 (d, *J* = 260.8 Hz), 155.0, 144.1, 130.3, 126.1, 124.5 (d, *J* = 9.1 Hz), 117.1 (d, *J* = 23.2 Hz), 58.9, 53.8, 26.8; MS: *m/z* 270 (M^+).

Anal. Calcd for $C_{11}H_{11}FN_2O_5$: C, 48.89; H, 4.10; N, 10.37. Found: C, 48.92; H, 4.10; N, 10.36.

1-(2-Chloro-5-nitrophenoxy)-2-propanone (22).

Ester **22** (0.95 g, 94%) was prepared as above from **21** (1.00 g, 4.38 mmol) isolated asa yellow solid; mp 85–87 ^{o}C. IR: 1728, 1525, 1348 cm^{-1}; ^{1}H NMR: δ 7.86 (dd, *J* = 8.8, 2.4 Hz, 1 H), 7.64 (d, *J* = 2.4 Hz, 1 H), 7.58 (d, *J* = 8.8 Hz, 1 H), 4.74 (s, 2 H), 2.39 (s, 3 H); ^{13}C NMR: δ 202.7, 153.6, 147.1, 130.8, 130.5, 117.3, 107.9, 73.4, 26.7; MS: *m/z* 229, 231 (*ca* 3:1, M^+)

Anal. Calcd for $C_9H_8ClNO_4$: C, 47.06; H, 3.49; N, 6.10. Found: C, 47.11; H, 3.52; N, 6.07.

Representative Procedure for Reductive Amination-S_NAr Cyclizations: (±)-Methyl 1-Benzyl-6-nitro-1,2,3,4-tetrahydroquinoline-4-carboxylate (23a).

The procedure of Bunce and Nago was used.[28] In a 50-mL, one-necked, round-bottomed flask, a solution of **12** (100 mg, 0.39 mmol) and benzylamine (51 mg, 0.52 mL, 0.47 mmol) in CH_3OH (4 mL) was stirred for 30 min, and $NaBH_3CN$ (21 mg, 0.33 mmol) was added. This was followed by two additional portions of $NaBH_3CN$ (7 mg, 0.11 mmol) at 12 h intervals. Stirring was continued for 48 h, and the crude reaction mixture was added to saturated NaCl and extracted with ether (3x). The combined ether extracts were dried ($MgSO_4$), concentrated under vacuum and purified by PTLC using 20% ether in hexanes. Band 1 gave **23a** (114 mg, 90%) as a yellow oil. IR: 1734, 1522, 1348 cm^{-1}; ^1H NMR: δ 8.06 (d, *J* = 2.7 Hz, 1 H), 7.93 (dd, *J* = 9.3, 2.7 Hz, 1 H), 7.36 (t, *J* = 7.3 Hz, 2 H), 7.28 (t, *J* = 7.3 Hz, 1 H), 7.18 (d, *J* = 7.3 Hz, 2 H), 6.51 (d, *J* = 9.3 Hz, 1 H), 4.63 (s, 2 H), 3.89 (apparent t, *J* = 4.2 Hz, 1 H), 3.75 (s, 3 H), 3.74 (m, 1 H), 3.44 (dddd, *J* = 12.6, 4.8, 3.7, 1.3 Hz, 1 H), 2.39 (dq, *J* = 13.5, 3.7 Hz, 1 H), 2.09 (ddt, *J* = 13.5, 11.7, 4.8 Hz, 1 H); ^{13}C NMR: δ 173.2, 149.8, 136.7, 136.0, 129.0, 127.5, 126.7, 126.1, 125.5, 117.1, 110.2, 55.0, 52.5, 46.7, 42.1, 23.4; MS: *m/z* 235 ($M^+-C_7H_7$).

Anal. Calcd for $C_{18}H_{18}N_2O_4$: C, 66.26; H, 5.52; N, 8.59. Found: C, 66.33; H, 5.56; N, 8.51.

(±)-Methyl 1-Hexyl-6-nitro-1,2,3,4-tetrahydroquinoline-4-carboxylate (23b).

Racemic ester **23b** (92 mg, 74%) was prepared as above from **12** (100 mg, 0.39 mmol) and hexylamine (47 mg, 0.062 mL, 0.47 mmol) isolated asa yellow solid; mp 60–62 ^{o}C. IR: 1735, 1522, 1346 cm^{-1}; ^{1}H NMR: δ 8.02 (m, 2 H), 6.55 (d, *J* = 9.9, Hz, 1 H), 3.80 (apparent t, *J* = 4.1 Hz, 1 H), 3.73 (s, 3 H), 3.61 (td, *J* = 12.6, 3.7 Hz, 1 H), 3.35 (m, 3 H), 2.33 (dq, *J* = 13.6, 3.6 Hz, 1 H), 1.96 (ddt, *J* = 13.6, 11.6, 4.9 Hz, 1 H), 1.63 (m, 2 H), 1.33 (m, 6 H), 0.90 (t, *J* = 6.6 Hz, 3 H); ^{13}CNMR: δ 173.3, 149.5, 135.9, 126.9, 125.5, 116.7, 109.5, 52.4, 51.7, 46.2, 41.9, 31.5, 26.6, 26.2, 23.2, 22.5, 13.9; MS: *m/z* 249 ($M^{+}-C_5H_{11}$).

Anal. Calcd for $C_{17}H_{24}N_2O_4$: C, 63.75; H, 7.50; N, 8.75. Found: C, 63.74; H, 7.51; N, 8.73.

(±)-Methyl 1-Isobutyl-6-nitro-1,2,3,4-tetrahydroquinoline-4-carboxylate (23c).

Racemic ester **23c** (101 mg, 89%) was prepared as above from **12** (100 mg, 0.39 mmol) and isobutylamine (34 mg, 0.047 mL, 0.47 mmol)isolated asa yellow oil. IR: 1735, 1522, 1347 cm^{-1}; ^{1}H NMR: δ 8.02 (d, *J* = 2.7 Hz, 1 H), 7.99 (dd, *J* = 9.2, 2.7 Hz, 1 H), 6.55 (d, *J* = 9.2 Hz, 1 H), 3.81 (apparent t, *J* = 4.2 Hz, 1 H), 3.73 (s, 3 H), 3.65 (td, *J* = 11.7, 3.7 Hz, 1 H), 3.36 (dm, *J* = 12.6 Hz, 1 H), 3.19 (ddd, *J* = 23.6, 14.6, 7.3 Hz, 2 H), 2.32 (dq, *J* = 13.6, 3.7 Hz, 1 H), 2.13 (nonet, *J* = 6.7 Hz, 1 H), 1.98 (ddt, *J* = 13.6, 11.7, 4.9 Hz, 1 H), 0.96 (d, *J* = 6.7 Hz, 3 H), 0.95 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR: δ 173.3, 149.8, 135.9, 126.9, 125.3, 116.7, 109.9, 59.4, 52.4, 47.4, 42.0, 26.7, 23.2, 20.2, 20.1; MS: *m/z* 249 ($M^{+}-C_3H_7$).

Anal. Calcd for $C_{15}H_{20}N_2O_4$: C, 61.64; H, 6.85; N, 9.59. Found: C, 61.75; H, 6.88; N, 9.53.

(±)-Methyl 1-Cyclohexyl-6-nitro-1,2,3,4-tetrahydroquinoline-4-carboxylate (23d).

Racemic ester **23d** (87 mg, 70%) was prepared as above from **12** (100 mg, 0.39 mmol) and cyclohexylamine (47 mg, 0.054 mL, 0.47 mmol) isolated asa yellow solid; mp 73–75 ^{o}C. IR: 1735, 1511, 1326 cm^{-1}; ^{1}H NMR: δ 8.01 (m, 2 H), 6.64 (d, *J* = 10.0 Hz, 1 H), 3.78 (apparent t, *J* = 4.5 Hz, 1 H), 3.72 (s, 3 H), 3.71 (dm, *J* = 12.7 Hz, 1 H), 3.40 (m, 1 H), 3.36 (td, *J* = 12.8, 3.8 Hz, 1 H), 2.34 (dq, *J* = 13.4, 3.8 Hz, 1 H), 1.95–1.69 (complex, 6 H), 1.62–1.30 (complex, 3 H), 1.26–1.09 (complex, 2 H); ^{13}C NMR: δ 173.2, 149.7, 135.6, 126.9, 125.5, 117.5, 109.6, 57.4, 52.3, 42.3, 38.8, 29.7, 29.4, 25.9, 25.7, 25.5, 23.5; MS: *m/z* 318 (M^{+}).

Anal. Calcd for $C_{17}H_{22}N_2O_4$: C, 64.13; H, 6.97; N, 8.80. Found: C, 64.17; H, 6.99; N, 8.76.

Methyl 4-Benzyl-7-nitro-3,4-dihydroquinoxaline-1(2*H*)-carboxylate (25a).

Ester **25a** (66 mg, 52%) was prepared as above from **18** (100 mg, 0.39 mmol) and benzylamine (51 mg, 0.052 mL, 0.47 mmol) isolated asa yellow solid; mp 102–103 ^{o}C. IR: 1709, 1522, 1330 cm^{-1}; ^{1}H NMR δ 8.41 (br s, 1 H), 7.86 (dd, *J* = 9.3, 2.6 Hz, 1 H), 7.38–7.25 (complex, 3 H), 7.18 (d, *J* = 6.6 Hz, 2 H), 6.60 (d, *J* = 9.3 Hz, 1 H), 4.65 (s, 2 H), 3.92 (t, *J* = 5.3 Hz, 2 H), 3.85 (s, 3 H), 3.58 (t, *J* = 5.3 Hz, 2 H); ^{13}CNMR: δ 154.3,

143.4, 136.9, 135.7, 129.1, 127.7, 126.2, 123.1, 122.2, 120.7, 110.1, 54.7, 53.5, 49.2, 40.7; MS: *m/z* 236 (M^+-C_7H_7).

Anal. Calcd for $C_{17}H_{17}N_3O_4$: C, 62.39; H, 5.20; N, 12.84. Found: C, 62.42; H, 5.23; N, 12.81.

Methyl 4-Hexyl-7-nitro-3,4-dihydroquinoxaline-1(2*H*)-carboxylate (25b).

Ester **25b** (78 mg, 62%) was prepared as above from **18** (100 mg, 0.39 mmol) and hexylamine (47 mg, 0.062 mL, 0.47 mmol) isolated asa yellow oil. IR: 1710, 1522, 1331 cm^{-1}; ^{1}HNMR δ 8.35 (br s, 1 H), 7.93 (dd, *J* = 9.3, 2.7 Hz, 1 H), 6.60 (d, *J* = 9.3 Hz, 1 H), 3.83 (s, 3 H), 3.83 (t, *J* = 5.3 Hz, 2 H), 3.49 (t, *J* = 5.3 Hz, 2 H), 3.38 (apparent t, *J* = 7.7 Hz, 2 H), 1.63 (quintet, *J* = 7.2 Hz, 2 H), 1.40–1.28 (complex, 6 H), 0.90 (distorted t, *J* = 6.8 Hz, 3 H); ^{13}C NMR: δ 155.1, 143.1, 136.2, 125.5, 122.3, 120.8, 109.3, 53.5, 51.6, 48.8, 40.5, 31.5, 26.6, 26.3, 22.6, 14.0; MS: *m/z* 250 (M^+−C_5H_{11}).

Anal. Calcd for $C_{16}H_{23}N_3O_4$: C, 59.81; H, 7.17; N, 13.08. Found: C, 59.90; H, 7.14; N, 12.99.

Methyl 4-Isobutyl-7-nitro-3,4-dihydroquinoxaline-1(2*H*)-carboxylate (25c).

Ester **25c** (63 mg, 55%) was prepared as above from **18** (100 mg, 0.39 mmol) and isobutylamine (34 mg, 0.047 mL, 0.47 mmol) isolated asa yellow oil. IR: 1709, 1524, 1328 cm^{-1}; ^{1}H NMR δ 8.37 (br s, 1 H), 7.92 (dd, *J* = 9.3, 2.4 Hz, 1 H), 6.61 (d, *J* = 9.3 Hz, 1 H), 3.84 (s, 3 H), 3.84 (t, *J* = 5.3 Hz, 2 H), 5.51 (t, *J* = 5.3 Hz, 2 H), 3.21 (d, 2 H, *J*

= 7.7 Hz, 2 H), 2.14 (nonet, *J* = 6.8 Hz, 1 H), 0.97 (d, *J* = 6.6 Hz, 6 H); ^{13}C NMR δ 154.4, 143.4, 136.3, 122.6, 122.1, 120.9, 109.8, 59.5, 53.5, 50.1, 40.4, 26.8, 20.3; MS: *m/z* 250 (M^+-C_3H_7).

Anal. Calcd for $C_{14}H_{19}N_3O_4$: C, 57.34; H, 6.48; N, 14.33. Found: C, 57.27; H, 6.44; N, 14.38.

Methyl 4-Cyclohexyl-7-nitro-3,4-dihydroquinoxaline-1(2*H*)-carboxylate (25d).

Ester **25d** (45 mg, 36%) was prepared as above from**18** (100 mg, 0.39 mmol) and cyclohexylamine (47 mg, 0.054 mL, 0.47 mmol) isolated asa yellow oil. IR: 1710, 1518, 1329 cm^{-1}; ^{1}H NMR: δ 8.33 (br s, 1 H), 7.93 (dd, *J* = 9.3, 2.8 Hz, 1 H), 6.68 (d, *J* = 9.3 Hz, 1 H), 3.83 (s, 3 H), 3.78 (t, *J* = 5.2 Hz, 2 H), 3.72 (tt, *J* = 11.4, 3.3 Hz, 1 H), 3.43 (t, *J* = 5.2 Hz, 2 H), 1.98–1.70 (complex, 5 H), 1.58–1.32 (complex, 3 H), 1.20 (m, 2 H); ^{13}C NMR: δ 154.2, 143.4, 135.9, 123.3, 122.4, 120.9, 109.5, 57.1, 53.4, 42.2, 40.7, 29.4, 25.7, 25.5; MS: *m/z* 319 (M^+).

Anal. Calcd for $C_{16}H_{21}N_3O_4$: C, 60.18; H, 6.58; N, 13.17. Found: C, 60.31; H, 6.62; N, 13.05.

(±)-Methyl 4-Benzyl-3-methyl-7-nitro-3,4-dihydroquinoxaline-1(2*H*)-carboxylate (26a).

Racemic ester **26a** (110 mg, 83%) was prepared as above from **19** (105 mg, 0.39 mmol) and benzylamine (51 mg, 0.52 mL, 0.47 mmol) isolated asa yellow solid; mp 101–103

^{o}C. IR: 1710, 1520, 1348 cm^{-1}; ^{1}H NMR: δ 8.47 (br s, 1 H), 7.81 (dd, *J* = 9.3, 2.7 Hz, 1 H), 7.39–7.24 (complex, 3 H), 7.15 (d, *J* = 7.0 Hz, 2 H), 6.48 (d, *J* = 9.3 Hz, 1 H), 4.70 (d, *J* = 17.4 Hz, 1 H), 4.61 (d, *J* = 17.4 Hz, 1 H), 4.38 (br d, *J* = 13.2 Hz, 1 H), 3.88 (s, 3 H), 3.80 (m, 1 H), 3.37 (dd, *J* = 13.2, 2.9 Hz, 1 H), 1.26 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR: δ 154.8, 142.9, 136.8, 136.1, 129.0, 127.6, 125.9, 122.9, 122.1, 120.1, 110.5, 54.3, 53.6, 52.9, 45.8, 17.6; MS: *m/z* 250 (M^{+}-C_7H_7).

Anal. Calcd for $C_{18}H_{19}N_3O_4$: C, 63.34; H, 5.57; N, 12.32. Found: C, 63.29; H, 5.58; N, 12.35.

(±)-Methyl 4-Hexyl-3-methyl-7-nitro-3,4-dihydroquinoxaline-1(2*H*)-carboxylate (26b).

Racemic ester **26b** (90 mg, 69%) was prepared as above from **19** (105 mg, 0.39 mmol) and hexylamine (47 mg, 0.062 mL, 0.47 mmol) isolated asa yellow oil. IR: 1710, 1522, 1353 cm^{-1}; ^{1}H NMR: δ 8.41 (br s, 1 H), 7.92 (dd, *J* = 9.3, 2.8 Hz, 1 H), 6.55 (d, *J* = 9.3 Hz, 1 H), 4.34 (dd, *J* = 13.1, 1.8 Hz, 1 H), 3.85 (s, 3 H), 3.69 (m, 1 H), 3.43 (m, 1H), 3.27 (m, 1 H), 3.16 (dd, *J* = 13.1, 3.0 Hz, 1 H), 1.63 (m, 2 H), 1.40–1.28 (complex, 6 H), 1.20 (d, *J* = 6.4 Hz, 3 H), 0.91 (distorted t, *J* = 7.0 Hz, 3 H); ^{13}C NMR: δ 154.7, 142.4, 135.9, 122.4, 122.0, 120.2, 109.3, 53.7, 53.4, 49.7, 45.5, 31.5, 26.7, 26.6, 22.5, 17.6, 13.9; MS: *m/z* 264 (M^{+}−C_5H_{11}).

Anal. Calcd for $C_{17}H_{25}N_3O_4$: C, 60.90; H, 7.46; N, 12.54. Found: C, 61.01; H, 7.49; N, 12.49.

(±)-Methyl 4-Isobutyl-3-methyl-7-nitro-3,4-dihydroquinoxaline-1(2*H*)-carboxylate (26c).

Racemic ester **26c** (90 mg, 75%) was prepared as above from **19** (105 mg, 0.39 mmol) and isobutylamine (34 mg, 0.047 mL, 0.47 mmol) isolated asa yellow solid; mp 109–110 ^{o}C. IR: 1709, 1521, 1354 cm^{-1}; ^{1}H NMR: δ 8.46 (br s, 1 H), 7.90 (dd, *J* = 9.3, 2.7 Hz, 1 H), 6.56 (d, *J* = 9.3 Hz, 1 H), 4.39 (dd, *J* = 13.0, 1.9 Hz, 1 H), 3.86 (s, 3 H), 3.70 (m, 1 H), 3.46 (dd, *J* = 14.5, 5.3 Hz, 1 H), 3.23 (dd, *J* = 13.1, 2.8 Hz, 1 H), 2.91 (dd, *J* = 14.8, 9.5 Hz, 1 H), 2.15 (m, 1 H), 1.17 (d, *J* = 6.4 Hz, 3 H), 0.964 (d, *J* = 6.8 Hz, 3 H), 0.960 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR: δ 154.8, 142.4, 136.0, 122.2, 121.8, 120.2, 109.9, 56.9, 53.9, 53.4, 45.2, 26.6, 20.1, 16.6; MS: *m/z* 264 ($M^{+}-C_3H_7$).

Anal. Calcd for $C_{15}H_{21}N_3O_4$: C, 58.63; H, 6.84; N, 13.68. Found: C, 58.59; H, 6.82; N, 13.73.

(±)-Methyl 4-Cyclohexyl-3-methyl-7-nitro-3,4-dihydroquinoxaline-1(2*H*)-carboxylate (26d).

Racemic ester **26d** (74 mg, 57%) was prepared as above from **19** (105 mg, 0.39 mmol) and cyclohexylamine (47 mg, 0.054 mL, 0.47 mmol) isolated asa yellow oil. IR: 1709, 1511, 1346 cm^{-1}; ^{1}H NMR: δ 8.50 (br s, 1 H), 7.91 (dd, *J* = 9.5, 2.8 Hz, 1 H), 6.71 (d, *J* = 9.5 Hz, 1 H), 4.43 (d, *J* = 12.7 Hz, 1 H), 3.93 (m, 1 H), 3.86 (s, 3 H), 3.72 (tt, *J* = 11.4, 3.3 Hz, 1 H), 2.89 (dd, *J* = 13.0, 2.4 Hz, 1 H), 2.10–1.62 (complex, 5 H), 1.60–1.32 (complex, 3 H), 1.21 (m, 2 H), 1.14 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR: δ 154.7, 141.8, 135.9,

122.6, 121.6, 120.4, 110.3, 58.0, 53.4, 47.3, 45.9, 31.1, 29.6, 26.0, 25.9, 25.5, 19.5; MS: *m/z* 318 (M^+-CH_3).

Anal. Calcd for $C_{17}H_{23}N_3O_4$: C, 61.26; H, 6.91; N, 12.61. Found: C, 61.39; H, 6.94; N, 12.51.

(±)-N-**Benzyl-1-(2-chloro-5-nitrophenoxy)-2-propanamine (28).**

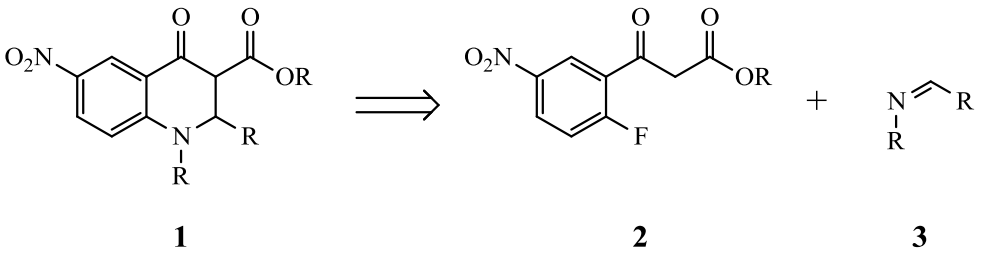
Racemic amine **28** (58 mg, 46%) was prepared as above from **22** (90 mg, 0.39 mmol) and benzylamine (51 mg, 0.52 mL, 0.47 mmol) isolated asan oil. IR: 3321, 1525, 1345 cm^{-1}; ^{1}H NMR: δ 7.78 (dd, *J* = 8.6, 2.6 Hz, 1 H), 7.74 (d, *J* = 2.4 Hz, 1 H), 7.50 (d, *J* = 8.6 Hz, 1 H), 7.39- 7.20 (complex, 5 H), 4.12 (m, 2 H), 3.97 (d, *J* = 13.6 Hz, 1 H), 3.86 (d, *J* = 13.6 Hz, 1 H), 3.25 (m, 1 H), 2.04 (br s, 1 H), 1.25 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR: δ 154.6, 147.2, 140.2, 130.3, 128.4, 128.1, 127.9, 127.0, 116.3, 107.7, 73.7, 51.2, 51.1, 17.2,; MS: *m/z* 320, 322 (ca 3:1, M^+).

CHAPTER III

SYNTHESIS OF HIGHLY SUBSTITUTED 1,2,3,4-TETRAHYDROQUINOLINES VIA A TANDEM IMINE ADDITION-S_NAr REACTION.

Introduction

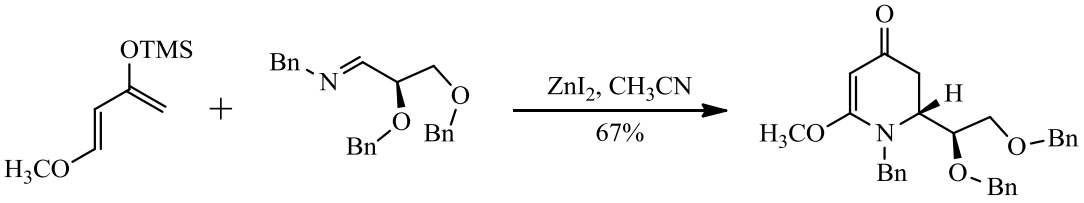
It was envisioned that highly substituted 1,2,3,4-tetrahydroquinolines could be made through a tandem, imine addition-S_NAr reaction. The retrosynthesis depicted in Figure 1 illustrates how a variety of 1,2,3,4-tetrahydroquinolines **1** might be produced from a β-ketoester **2** and a variety of imines **3**. The imines could be prepared from the corresponding aldehyde and amine. As with other tandem reactions involving nucleophilic aromatic substitution (S_NAr) reactions, the β-ketoester has a nitro group incorporated in the structure to activate the aromatic ring towards nucleophilic substitution. Generation of the enolate of the β-ketoester may be necessary to initiate the imine addition portion of the tandem reaction. A non-nucleophilic base would be required to generate the enolate as the activated aromatic ring would be sensitive to nucleophilic bases, such as 1^o or 2^o amines, alkoxide or hydroxide. This tandem imine addition-S_NAr reaction presents an opportunity to generate a large library of highly substituted 1,2,3,4-tetrahydroquinolines quickly from readily available starting materials.



1 **2** **3**

Figure 1. Retrosynthesis of imine addition-S_NAr reaction.

Examples of tandem reactions using imines as reactants are relatively sparse in the literature, and many require the use of a Lewis acid or catalyst to facilitate the reaction. Badorrey and coworkers[29] have developed a diastereoselective tandem Mannich-Michael reaction for the synthesis of piperidine ring systems. Under zinc-iodide catalyzed conditions the authors were able to react Danishefsky's diene (**4**) with an *N*-benzylimine **5**, derived from protected (*R*)-glyceraldehyde, providing a new approach to the homochiral piperidine **6**. To achieve acceptable yields the reaction required the use of acetonitrile as the solvent and the presence of zinc iodide as a Lewis acid. The stereoselectivity was attributed to the complex between the chelation of zinc iodide and the chiral imine.



4 **5** **6**

Figure 2. Badorrey's tandem Mannich-Michael reaction.

Jaber and co-workers[30] have reported a one-pot cascade reaction that uses samarium diiodide as a precatalyst. The reaction started by reacting cyclopentenone **7** and silyl ketene acetal **8** in the presence of a suspension of samarium diiodide (10 mol%) in methylene chloride to give the Michael adduct **9**. After 30 minutes, ethyl glyoxalate (*N*-*p*-anisyl) imine (**10**) was added to the reaction causing a Mukaiyama reaction to give the disubstituted cyclopentanone adducts **11**and **12** in an isolated yield of 50% with a 70/30 diastereomeric ratio of **11**/**12**.

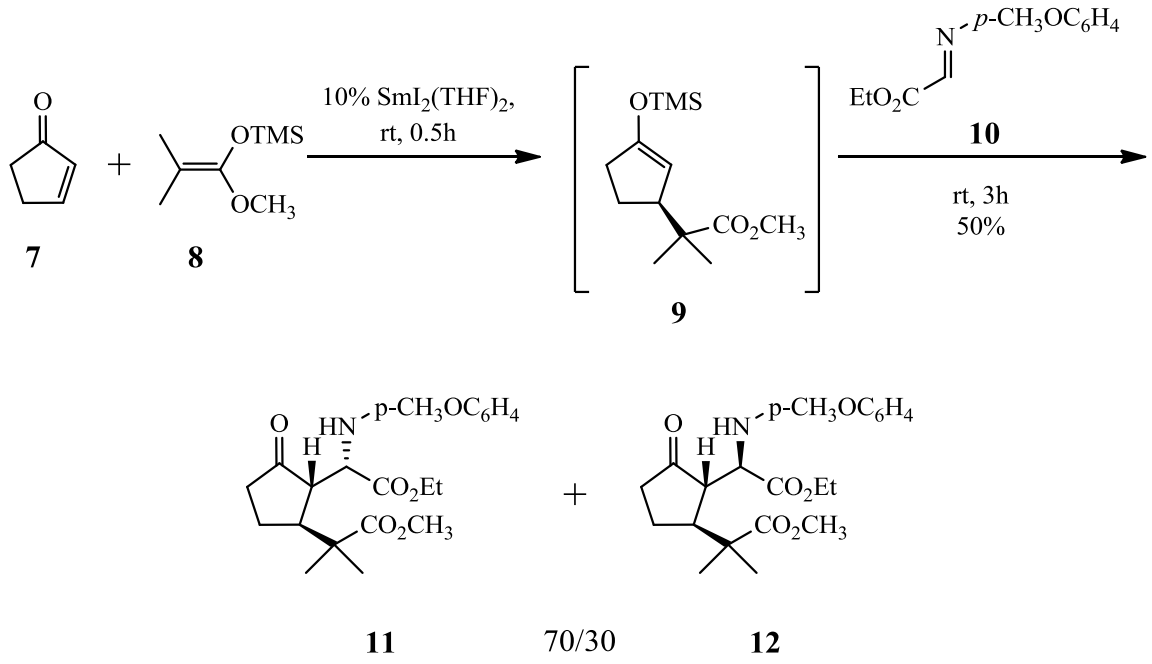


Figure 3. Jaber's one-pot reaction using samarium diiodide.

Another example of a tandem reaction using imines has been carried out by Raw and coworkers[31] to used tethered imine–enamines to convert 1,2,4-triazines into highly substituted pyridines through a series of cascading reactions. The tandem reaction began with a Diels–Alder reaction between a disubsituted 1,2,4-triazine **13** and the imine-enamine **14** to give the intermediate **15**. Subsequent bond rearrangements and

eliminations then led to intermediate **16**. A final elimination-rearomatization gave the disubstituted pyridine products **17** in moderate to excellent yields.

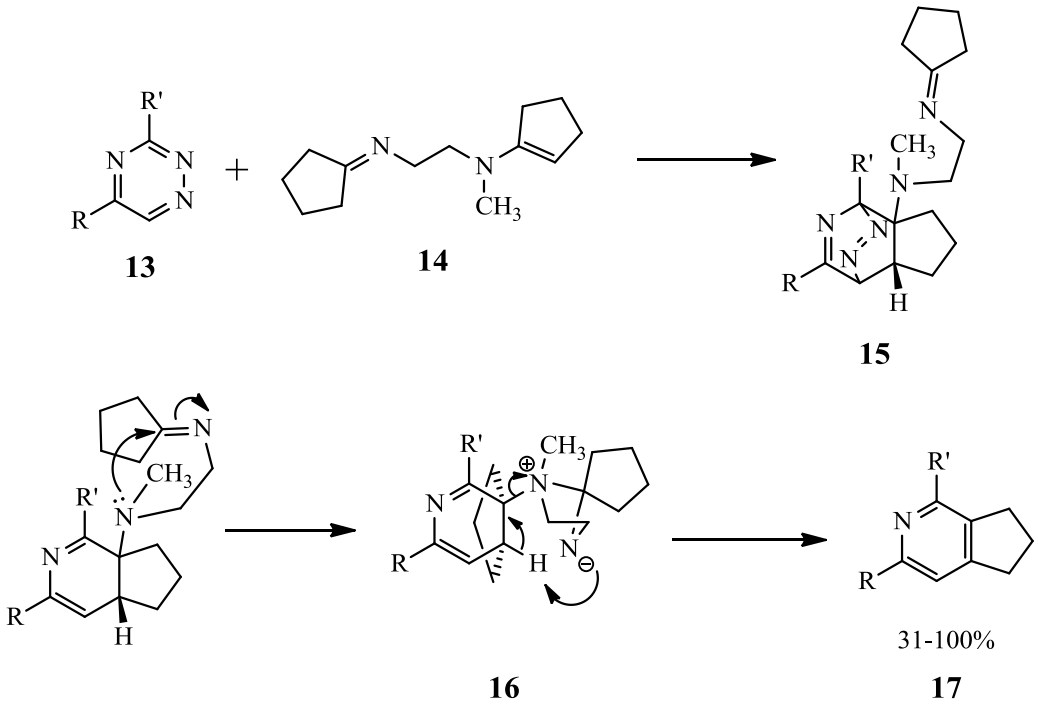


Figure 4. Raw's synthesis of pyridines using tethered imine-enamines.

Lu and coworkers[32] have developed a copper-catalyzed three-component reaction that furnished a new class of *N*-sulfonyl-2-alkylidene-1,2,3,4-tetrahydropyrimidines **18** in moderate to good yields. The CuBr-catalyzed addition of sulfonyl azide **20** to phenylacetylene **19** formed ketenimine intermediate **21**. This intermediate then underwent cyclization initiated by nucleophilic addition of the α,β-unsaturated imine **22** to give the tetrahydropyrimidine product **18**.

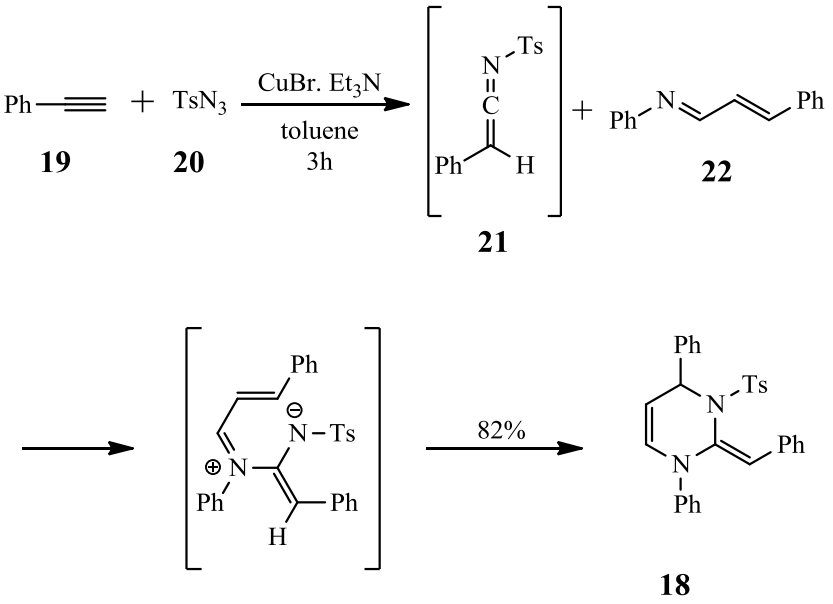


Figure 5. Lu's copper-catalyzed three-component reaction.

Results

Synthesis of Precursors

The needed substrates for the tandem imine addition-S_NAr reaction were synthesized as illustrated in Figure 6. The synthesis began by nitrating the commercially available 2-fluorobenzaldehyde (**23**) to give 2-fluoro-5-nitrobenzaldehyde (**24)**. The aldehyde functional group was oxidized using freshly prepared Jones reagent[33] to afford the corresponding carboxylic acid **25**. Several attempts were made to acylate Meldrum's acid using the acid chloride **26** derived from **25** by the method of Yonemitsu and co-workers.[34] The reaction, however, failed to give the desired product. It was found that acylation was possible by reacting the acid chloride **26** with the dianion of alkyl hydrogen malonate **27** at low temperature.[35] This sequence of reactions consistently gave the desired β-ketoesters **28** and **29** in acceptable yields, presented in Table 1. When both **28** and **29** were analyzed by ^{1}H NMR, it was discovered that the enol was the preferred

tautomer as evidenced by the broad singlet at δ 12.8, corresponding to the hydrogen bonded OH of the enol. This, we believed, would not be an issue as the enol should also deprotonate to give the needed enolates.

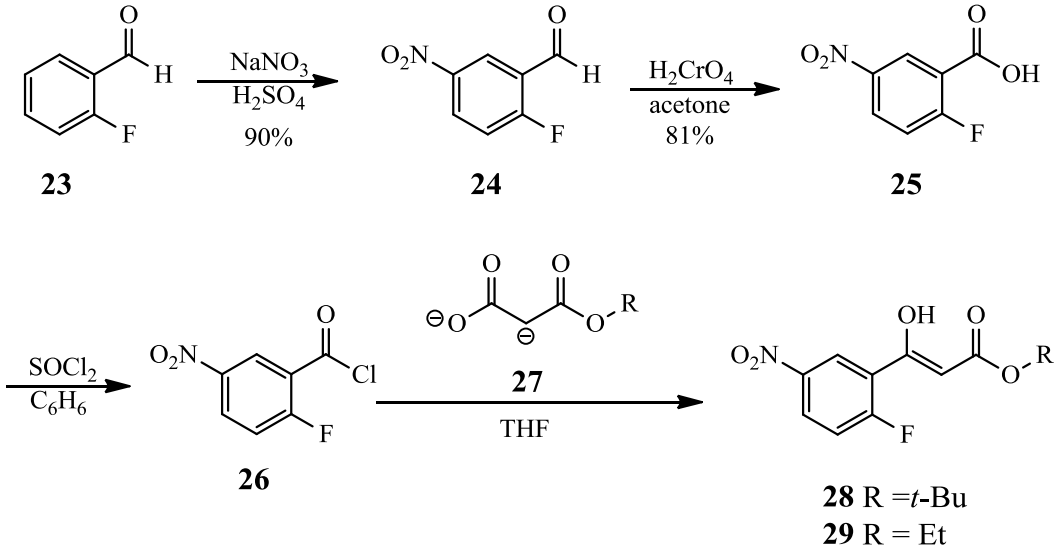


Figure 6. Synthesis of the β-ketoesters.

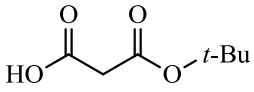
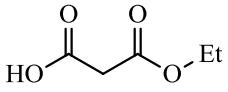
starting material	R	product	yield
	*t*-Bu	**28**	94%
	Et	**29**	72%

Table 1. Synthesis of the β-ketoesters.

At the start of this project there were concerns about using an imine as a reactant in the tandem reaction. First, the imine C=N is easily hydrolyzed and could degrade back to its starting aldehyde and amine in the presence of excess water. If the degradation

occured, then the proposed tandem reaction would not be possible. Additionally, the amine formed from the degradation could undergo a S_NAr reaction with the aromatic ring of the β-ketoesters **28** and **29**. These problems should be avoidable by using stabilized imines under anhydrous conditions for the tandem reaction.

Benzaldehyde (**30**) and its derivatives are known to form stable imines.[36] These imines are stabilized by conjugation between the C=N and the aromatic ring, which allows the imines to be isolated and used in reactions. Many studies have been conducted on the stability of these types of imines in aqueous solutions.[37] Aromatic imines have been generated by several methods, from simple condensation between an aldehyde and an amine[38] to the pyrolysis of alkyl azides.[39] It was our plan to use the simplest set of conditions and a minimal workup. This would reduce the possibility of decomposing the imine and keep the synthesis of the 1,2,3,4-tetrahydroquinoline relatively straightforward.

To develop the optimum conditions for imine formation, benzaldehyde (**30**) and benzylamine (**31**) were selected for generating the aromatic imines. The ability to see both of these reactants on a TLC plate would enable accurate monitoring of the reaction progress. It was found that mixing a 1:1.2 ratio of **30** and **31** in hexanes produced a new spot on the TLC plate with complete consumption of the starting amine. It is essential not to have excess amine present, as this could result in an undesirable S_NAr side reaction between the amine and the aromatic ring of the β-ketoesters **28** and **29**. The imine **32** was isolated by removal of the solvent and water under vacuum using a rotary evaporator followed by use of a high vacuum pump. The structure was confirmed by ^1H NMR and the imine was used immediately in the next reaction.

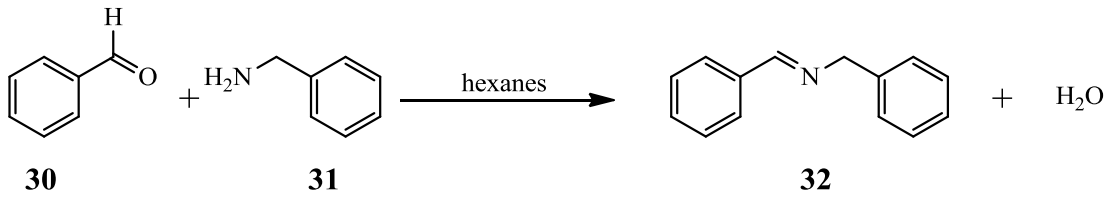


Figure 7. Imine generation in hexanes.

Conducting the Tandem Imine Addition-S_NAr Reaction

Once the needed substrates were acquired, an investigation into the tandem imine addition-S_NAr reaction was initiated. The results are summarized in Table 2. As discussed earlier, it was believed that the enolate of **28** would be necessary for addition to the imine. In the first attempt of the tandem reaction, one equivalent of oil-free, NaH (washed three times with hexanes) was used to generated the enolate of **28** in anhydrous *N*,*N*-dimethylformamide (DMF), followed by the addition freshly prepared imine **32**. This resulted in a complex mixture that could not be separated. In hopes that a milder base would produce fewer side reactions, the second attempt used one equivalent of anhydrous K_2CO_3 to generate the enolate of **28**, followed by addition of fresh imine **32**. The reaction was worked up and separated using preparative thin layer plate chromatography, but afforded only a minimal yield of the desired product **33**.

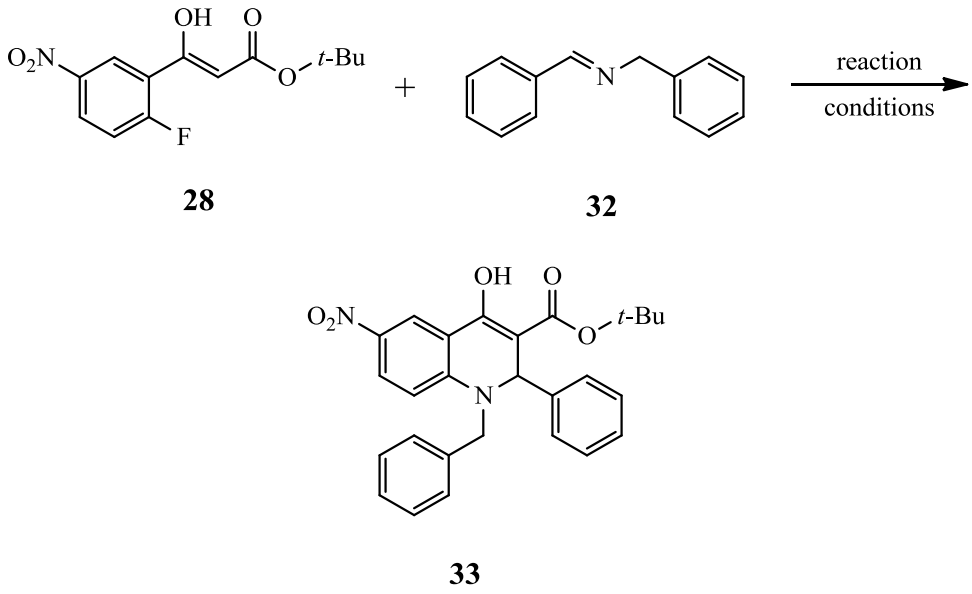


Figure 8. Initial tandem imine addition-S_NAr reaction.

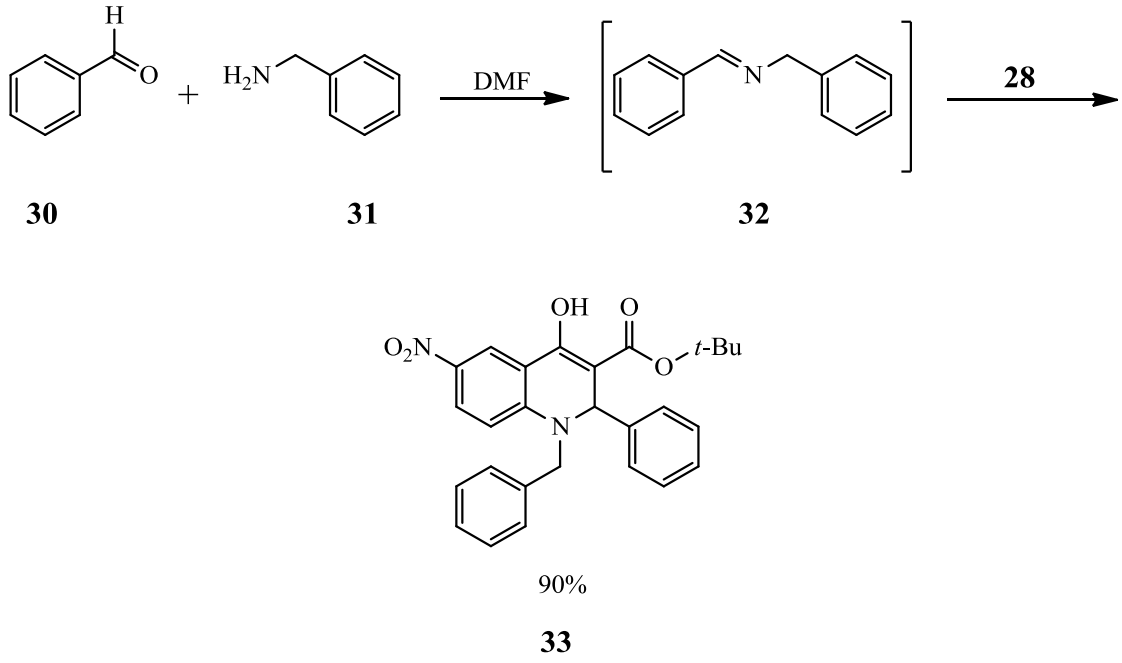
reaction conditions	results
Enolate generation with NaH followed by imine addition.	Complex mixture
Enolate generation with anhydrous K_2CO_3 followed by imine addition.	Low yield of **33** isolated
Addition of **32** to solution of **28** followed by anhydrous K_2CO_3.	Solution changed color before base addition and yield of **33** increase
Addition of **32** to solution of **28** without adding anhydrous K_2CO_3.	High yield of **33** formed with minimal purification

Table 2. Initial tandem imine addition-S_NAr reaction.

It was thought that generating the enolate in the presence of an imine would decrease the possibility of side reactions and improve the yield of **33**. This was accomplished by adding the base to the reaction last. When freshly prepared imine **32**

was added to an anhydrous DMF solution of β-ketoester **28**, followed by addition of anhydrous K_2CO_3, the yield of **33** increased significantly. During this run, we noticed the solution underwent a color change after **32** was added to the reaction and before the base was added. This led us to believe that the enolate of **28** may not be needed to initiate the tandem reaction. To test this hypothesis, freshly prepared imine **32** was added to an anhydrous DMF solution of the β-ketoester **28**. The solution instantly turned bright yellow upon this addition. After 6 hours the reaction was worked up using saturated NaCl solution and methylene chloride to yield the desired 1,2,3,4-tetrahydroquinoline **33** as a yellow solid. A ^{1}H NMR of the sample showed the reaction required minimal purification, and the product was isolated as the enol tautomer as evidenced by the presence of an enolic OH at δ 12.60 ppm.

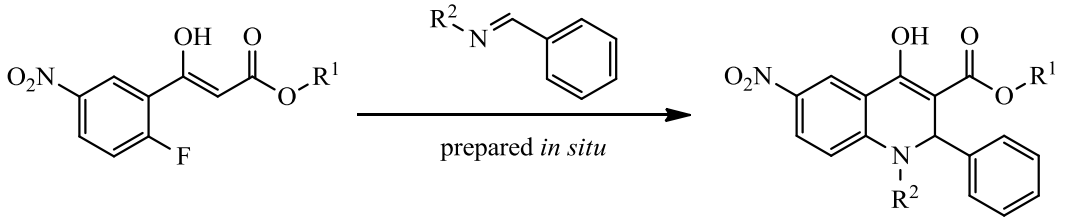
It was found that the imine formation, and subsequent tandem cyclization to form 1,2,3,4-tetrahydroquinolinones, could be conducted in the same reaction vessel. This procedure eliminated isolation of the imine from the method, making the synthesis more efficient. This was accomplished by reacting benzaldehyde (**30**) and benzylamine (**31**) together in a 1:1.2 ratio in anhydrous DMF to generate the imine **32**. The reaction was monitored by TLC until all of the benzylamine (**31**) was consumed. At this point, one equivalent of **28** was added and the color instantly changed to a bright yellow color. The reaction was allowed to stir for 6 hours and was then worked up to isolate the product **33** as a yellow solid in a 90% yield. The product was triturated with a small amount of ether and the product required no further purification.



30 **31** **32** **33**

Figure 9. Tandem imine addition-S_NAr reaction to give **33**.

Once these conditions were established, an array of substrates was used to expand the scope of the tandem reaction. First, aromatic imines were formed by reacting a variety of primary amines with benzaldehyde (**30**) in a 1:1.2 ratio in anhydrous DMF. Once the aromatic imines were formed in solution, the β-ketoesters **28** and **29** were added to the reactions. The reactions were worked up and the products were isolated and purified by trituration with ether to provide the pure compounds **33-37** and **38-42**, respectively. The yields for these reactions are given in Table 3.



28 (R^1 = *t*-Bu)
29 (R^1 = Et)

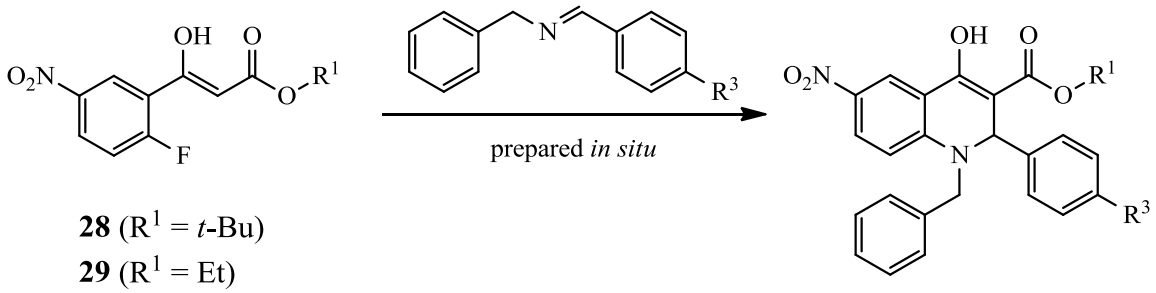
33 (R^1 = *t*-Bu, R^2 = CH_2Ph)
34 (R^1 = *t*-Bu, R^2 = *n*-C_6H_{13})
35 (R^1 = *t*-Bu, R^2 = *i*-C_4H_9)
36 (R^1 = *t*-Bu, R^2 = *c*-C_3H_5)
37 (R^1 = *t*-Bu, R^2 = $CH_2CH{=}CH_2$)
38 (R^1 = Et, R^2 = CH_2Ph)
39 (R^1 = Et, R^2 = *n*-C_6H_{13})
40 (R^1 = Et, R^2 = *i*-C_4H_9)
41 (R^1 = Et, R^2 = *c*-C_3H_5)
42 (R^1 = Et, R^2 = $CH_2CH{=}CH_2$)

Figure 10. Tandem reaction using various primary amines.

R^1	R^2	product	yield (%)
t-Bu	CH_2Ph	**33**	90
t-Bu	*n*-C_6H_{13}	**34**	93
t-Bu	*i*-C_4H_9	**35**	95
t-Bu	*c*-C_3H_5	**36**	79
t-Bu	$CH_2CH{=}CH_2$	**37**	75
Et	CH_2Ph	**38**	89
Et	*n*-C_6H_{13}	**39**	98
Et	*i*-C_4H_9	**40**	72
Et	*c*-C_3H_5	**41**	85
Et	$CH_2CH{=}CH_2$	**42**	97

Table 3. Tandem reaction using various primary amines.

Next, a number of substituted benzaldehydes was reacted as above with benzylamine (**31**) to generate a series of imines to be used in the synthesis. The reactions were monitored by TLC, and again, once the aromatic imines were formed, the β-ketoesters **28** and **29** were added to the reaction giving a yellow color change. The reactions were worked up and the products were isolated and purified by trituration with ether to give the desired products **43-45** and **46-48**, respectively. The yields for these reactions are given in Table 4.



28 (R^1 = *t*-Bu)
29 (R^1 = Et)

43 (R^1 = *t*-Bu, R^3 = OCH_3)
44 (R^1 = *t*-Bu, R^3 = F)
45 (R^1 = *t*-Bu, R^3 = CF_3)
46 (R^1 = Et, R^3 = OCH_3)
47 (R^1 = Et, R^3 = F)
48 (R^1 = Et, R^3 = CF_3)

Figure 11. Tandem reaction using various aromatic aldehydes.

R^1	R^3	product	yield (%)
t-Bu	H	**33**	90
t-Bu	OMe	**43**	82
t-Bu	F	**44**	97
t-Bu	CF_3	**45**	92
Et	H	**38**	89
Et	OMe	**46**	73
Et	F	**47**	92
Et	CF_3	**48**	55

Table 4. Tandem reaction using various aromatic aldehydes.

Following the success of the tandem imine addition-S_NAr reaction using *N*-benzylimines of aromatic aldehydes, it was believed that the tandem reaction might be extended to include the use of imines derived from aliphatic aldehydes. This would greatly expand the scope of the tandem imine addition-S_NAr reaction. The established procedure was first attempted using acetaldehyde (**49**) and benzylamine (**31**). These substrates were reacted in a 1:1.2 ratio in anhydrous DMF followed by the addition the β-ketoester **28**, resulting in an immediate color change. Unlike the previous cases the reaction required purification using preparative thin layer chromatography. The major band from the plate was determined to be the free amine addition product **50** from the simple S_NAr reaction of **28** with **31**.

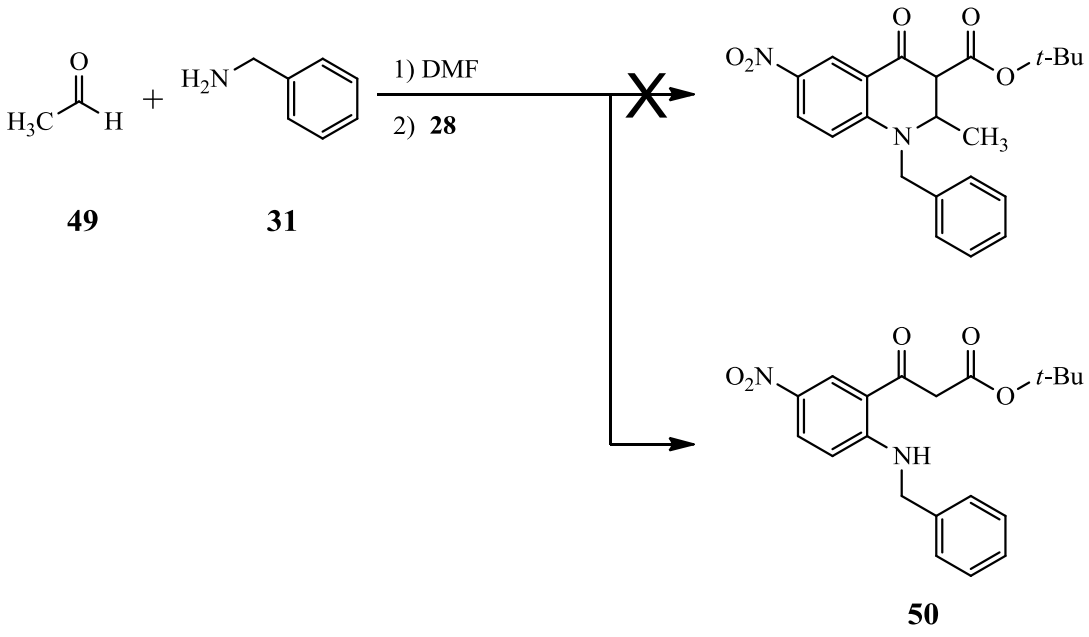
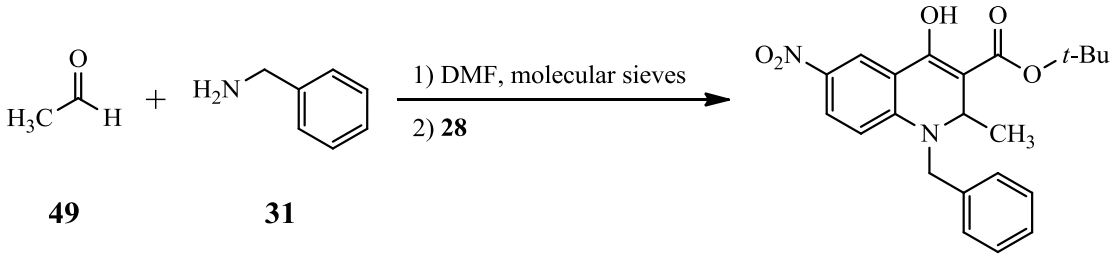


Figure 12. Attempted tandem reaction using acetaldehyde.

As discussed earlier, this type of problem was a concern when using non-stabilized imines. An investigation of the literature showed that stable aliphatic imines had been formed in solution by using 4 Å molecular sieves in the reaction.[40] Based on

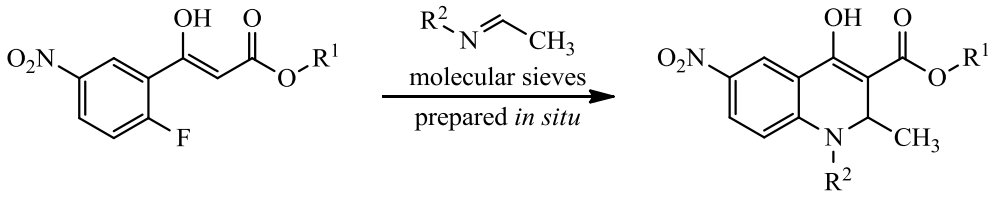
this report, we modified the procedure to include the use of 4 Å molecular sieves when generating aliphatic imines. Thus, benzylamine (**31**) and acetaldehyde (**49**) were reacted in a 1:1.2 ratio in anhydrous DMF in the presence of 4 Å molecular sieves. The β-ketoester **28** was added to the reaction, and the solution turned dark yellow instantly. The reaction was worked up and purified using thin layer chromatography to afford the desired 1,2,3,4-tetrahydroquinolinone **51** in a yield of 92%.



49 **31** **51**

Figure 13. Tandem reaction using acetaldehyde.

Using the new conditions, a variety of acetaldehyde imines could be used in the tandem reaction. The β-ketoesters **28** and **29** were added to the reactions, causing an instant change in the color of the solutions. The reactions were worked up; products were isolated and purified using thin layer chromatography to give the desired targets **51**-**55** and **56**-**60**, respectively. The yields for these reactions are given in Table 5.



28 (R^1 = *t*-Bu)
29 (R^1 = Et)

51 (R^1 = *t*-Bu, R^2 = CH_2Ph)
52 (R^1 = *t*-Bu, R^2 = *n*-C_6H_{13})
53 (R^1 = *t*-Bu, R^2 = *i*-C_4H_9)
54 (R^1 = *t*-Bu, R^2 = *c*-C_3H_5)
55 (R^1 = *t*-Bu, R^2 = $CH_2CH{=}CH_2$)
56 (R^1 = Et, R^2 = CH_2Ph)
57 (R^1 = Et, R^2 = *n*-C_6H_{13})
58 (R^1 = Et, R^2 = *i*-C_4H_9)
59 (R^1 = Et, R^2 = *c*-C_3H_5)
60 (R^1 = Et, R^2 = $CH_2CH{=}CH_2$)

Figure 14. Tandem reaction using various acetaldehyde imines.

R^1	R^2	product	yield (%)
t-Bu	CH_2Ph	**51**	92
t-Bu	*n*-C_6H_{13}	**52**	97
t-Bu	*i*-C_4H_9	**53**	81
t-Bu	*c*-C_3H_5	**54**	75
t-Bu	$CH_2CH{=}CH_2$	**55**	65
Et	CH_2Ph	**56**	96
Et	*n*-C_6H_{13}	**57**	94
Et	*i*-C_4H_9	**58**	89
Et	*c*-C_3H_5	**59**	95
Et	$CH_2CH{=}CH_2$	**60**	95

Table 5. Tandem reaction using various acetaldehyde imines.

In an effort to further expand the scope of the newly developed tandem imine addition-S_NAr reaction, we endeavored to determine if a ketone could be used to generate trisubstituted imines. This would result in 1,2,3,4-tetrahydroquinolines with geminal disubstitution at the C2 position of the ring. The reaction was first attempted with acetophenone (**61**) as the ketone, as this would provide a stabilized aromatic imine. Following the conditions established earlier for aromatic imines, **31** and **61** were reacted in a 1:1.2 ratio followed by the addition of **28**. The only product isolated from the reaction was the free amine addition product **50** observed previously. Several attempts to modify the reaction conditions, including addition of molecular sieves, increased reaction

temperature and solvent changes, did not result in the desired product. It is believed that the addition of the methyl group in the imine caused steric hindrance and prevented the initial imine addition step of the tandem reaction. This allowed the imine the opportunity to hydrolyze back to benzylamine (**31**), which then reacted with the aromatic ring of the β-ketoester **28** giving the observed product **50**.

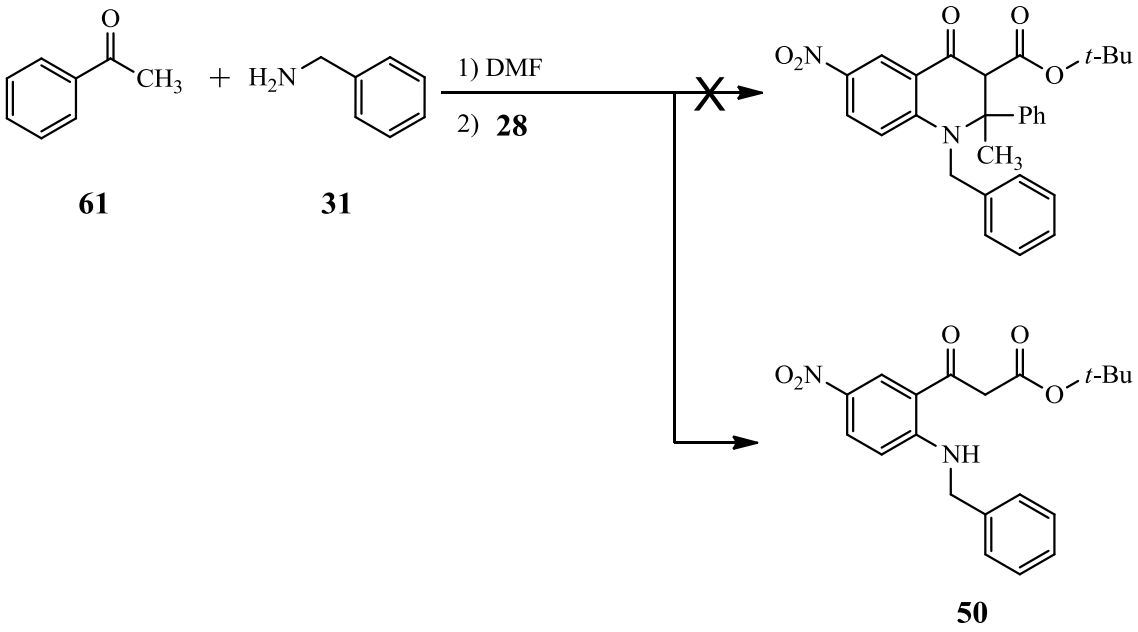


Figure 15. Attempted tandem reaction using acetophenone.

To reduce the amount of steric hindrance in the reaction, attempts were made to use the *N*-benzyl imines **63** derived from acetone in a tandem reaction. Following the procedure established for aliphatic imines, the imine of derived from acetone (**62**) and benzylamine (**31**) was generated in anhydrous DMF using 4 Å molecular sieves, followed by the addition of **28**. However, only the free amine addition product **50** was isolated from the reaction, and none of the desired heterocycle was formed. In a final attempt to generate the geminal dimethyl-substituted 1,2,3,4-tetrahydroquinoline, pure imine **63** was prepared and used for the tandem reaction. Acetone (**62**) and benzylamine (**31**) were

reacted together in benzene using a dean-stark trap to remove the water produced from the reaction, followed by vacuum distillation to give the pure imine **63**. However, when **63** was added to a anhydrous DMF solution of **28**, only the free amine addition product **50** was isolated. Again, it is believed that steric hindrance prevented the initial imine.

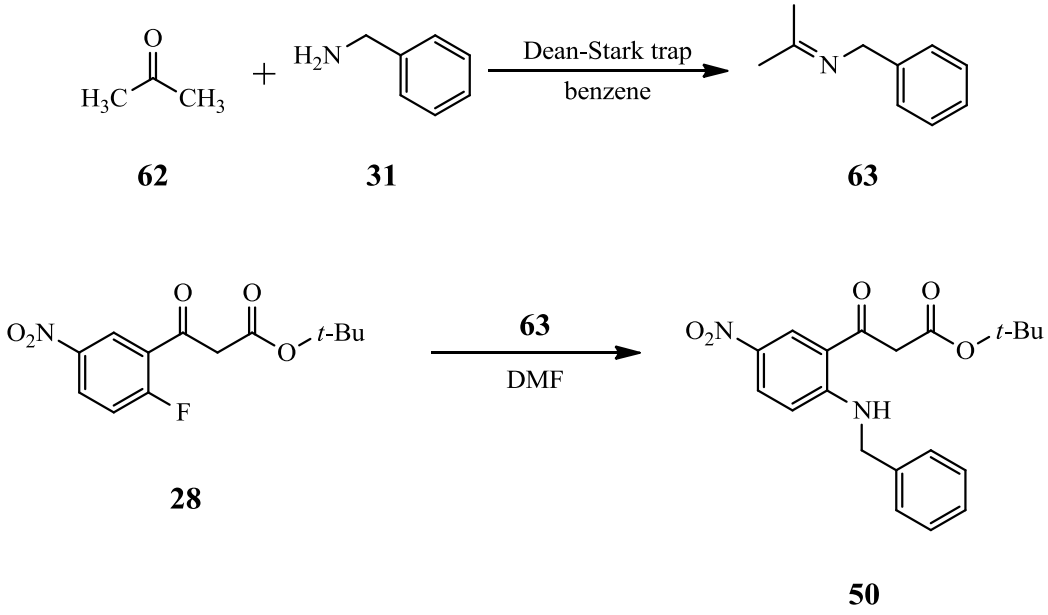


Figure 16. Attempted tandem reaction using pure imine of acetone.

Mechanism for the Tandem Imine Addition-S_NAr Reaction

There are two conceivable pathways the reactants could follow when generating 1,2,3,4-tetrahydroquinolinones. The first possibility is a proposed tandem imine addition-S_NAr reaction, the mechanism of which is illustrated in Figure 17. Electrons from the enol oxygen shift through the enol double bond and attack the electron deficient carbon of the imine double bond, increasing electron density on the nitrogen with a subsequent proton transfer. The resulting amine nitrogen is then in a position to displace the fluoro group on the aromatic ring, giving the keto form of the final product. The keto group then undergoes tautomerization to give the isolated product **33**.

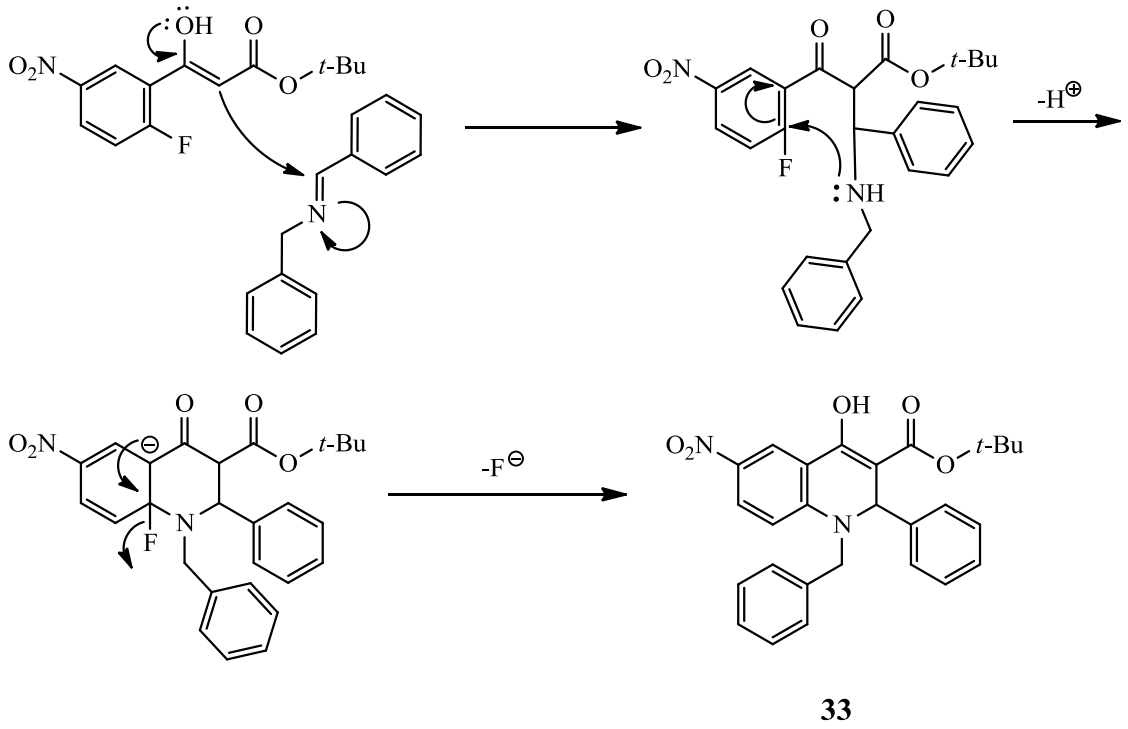


Figure 17. Tandem imine addition-S_NAr mechanism.

The second mechanism involves two possible pathways, both depicted in Figure 18. In each, an imine is not included in the pathway, but rather the starting amine and aldehyde. Pathway A begins with an aldol condensation between the benzaldehyde (**30**) and the β-ketoester **28** to give the intermediate **28a**. This could then undergo a tandem Michael addition-S_NAr reaction with benzylamine (**31**) to give the heterocyclic product **33**. There are a number of problems with this pathway: first, the aldol condensation reaction is relatively slow when compared to the S_NAr reaction between an amine and the activated aromatic ring; second, based on research in our laboratory the tandem Michael addition-S_NAr requires an increase in reaction temperature and reaction time.[41] Pathway B assumes that the S_NAr reaction will occur first between the β-ketoester **28** and benzylamine (**31**) to give the free amine addition intermediate **50**, which has been seen

before from the failed tandem reaction presented in Figures 15 and 16. This intermediate would then undergo a tandem aldol condensation-Michael addition reaction with benzaldehyde (**30**) to give the final product **33**.

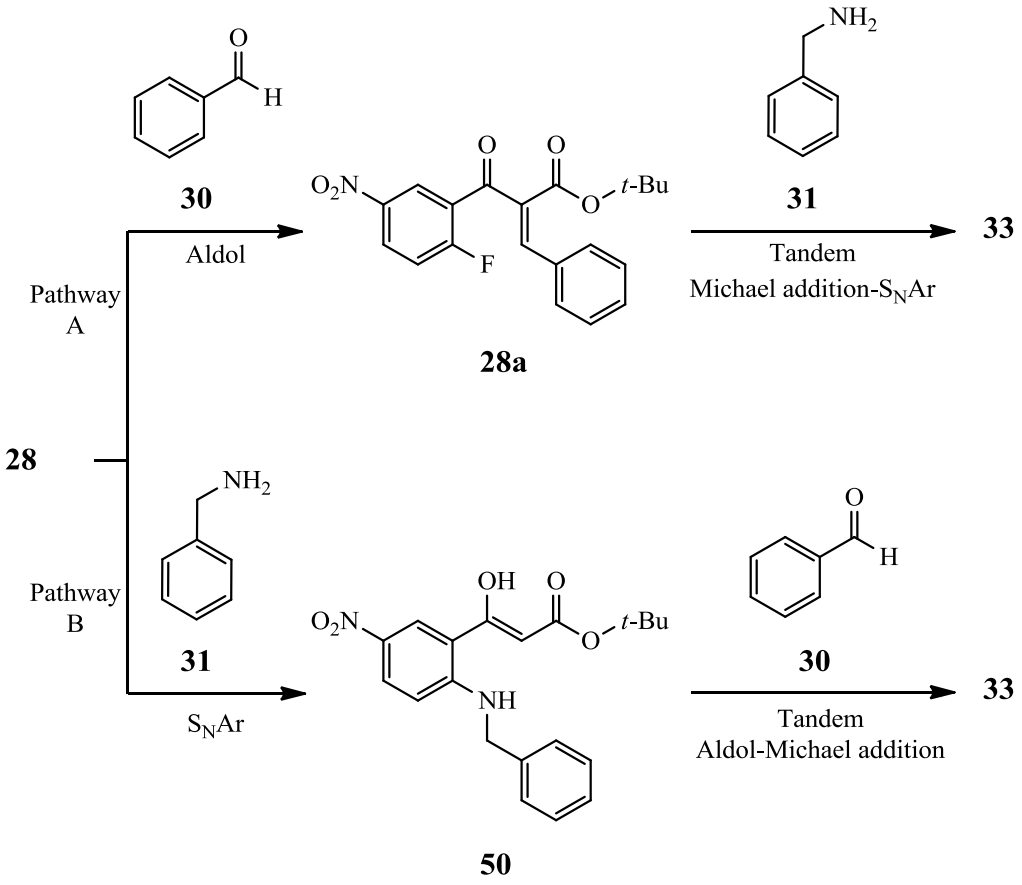
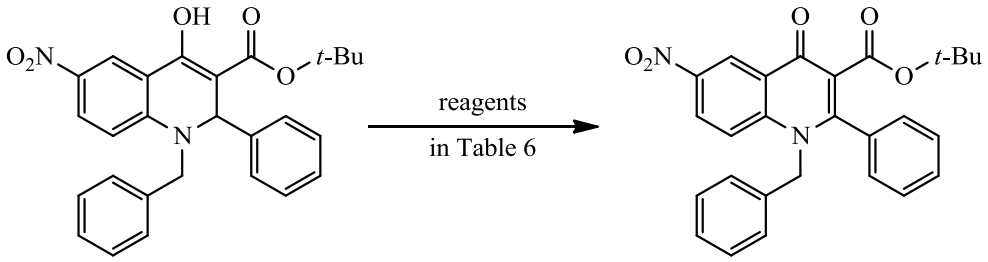


Figure 18. Alternative mechanisms.

To determine the possibility of pathway B, the intermediate **50** was generated and isolated by reacting the β-ketoester **28** with benzylamine (**31**). This intermediate was reacted with one equivalent of benzaldehyde (**30**) and stirred for 3 days at 50 ^{o}C, however, none of the desired product **33** was isolated. This led us to conclude that the imine is necessary for generating the 1,2,3,4-tetrahydroquinolinone and follows the mechanism presented in Figure 17.

Synthesis of 2,3-Dihydroquinolinone-3-carboxylate

In an attempt to elaborate the tandem products, it was thought that the 1,2,3,4-tetrahydroquinolinone ring structure could be converted to the corresponding 2,3-dihydroquinolinones through a double bond migration reaction. Using **33** as a test case, a number of literature procedures were tried in the effort to produce a double bond between carbons C2 and C3. The first reaction attempts used benzoquinone oxidizing agents chloranil and 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ)[42] in an effort to generate the desired compound **64.** However, only starting material was recovered from these reactions. The use of Br_2 and Et_3N[43] also failed to give the desired product. In a final try, MnO_2 was added in a 10-fold excess[44] as the oxidizing agent and product **64** was isolated in a 57% yield after 3 days.



33 **64**

Figure 19. Synthesis of 2,3-dihydroquinolinone **64**.

reagents	results
Chloranil	recovered starting material
2,3-Dichloro-5,6-dicyanobenzoquinone (DDQ)	recovered starting material
Br_2, then Et_3N	no recovered starting material or product
MnO_2	**64** isolated in 57% yield

Table 6. Synthesis of 2,3-dihydroquinolinone **64**.

Alkylation-Decarboxylation of Tandem Product

The tandem imine addition-S_NAr reaction provides a convenient method for making a multitude substituted 1,2,3,4-tetrahydroquinolinones. It was imagined that these products might be elaborated by introducing additional substitution onto the tetrahydroquinolinone ring. An alkyation-decarboxylation procedure at the C3 position of the ring would increase the versatility of the tandem reaction products, providing a convenient route to trisubstituted 1,2,3,4-tetrahydroquinolinones.

The 1,2,3,4-tetrahydroquinolinone **33** was used as an example case for the alkylation procedure. Deprotonation of the enol **33**, with potassium carbonate and alkylation with methyl iodide gave product **65** as the only product in a 94% yield. The stereochemistry of this alkylation would be anticipated to give the *trans* isomer based on the studies of Zimmerman and co-workers.[45] This is because the CH_3 approaches from the less hindered side of the structure, opposite of the C2 phenyl. The *tert*-butyl ester was converted to the corresponding carboxylic acid (**66**) using CF_3CO_2H. Decarboxylation

then provided a quick and efficient route to highly substituted (±)-1-benzyl-3-methyl-6-nitro-2-phenyl-2,3-dihydroquinolin-4(1*H*)-one (**67**). To determine the stereochemistry about the C2 and C3 positions, an X-ray analysis of **67** was conducted. As seen in Figure 21, the phenyl and methyl substituents have the *cis* orientation, resulting from the protonation on the face opposite of the C2 phenyl.[45]

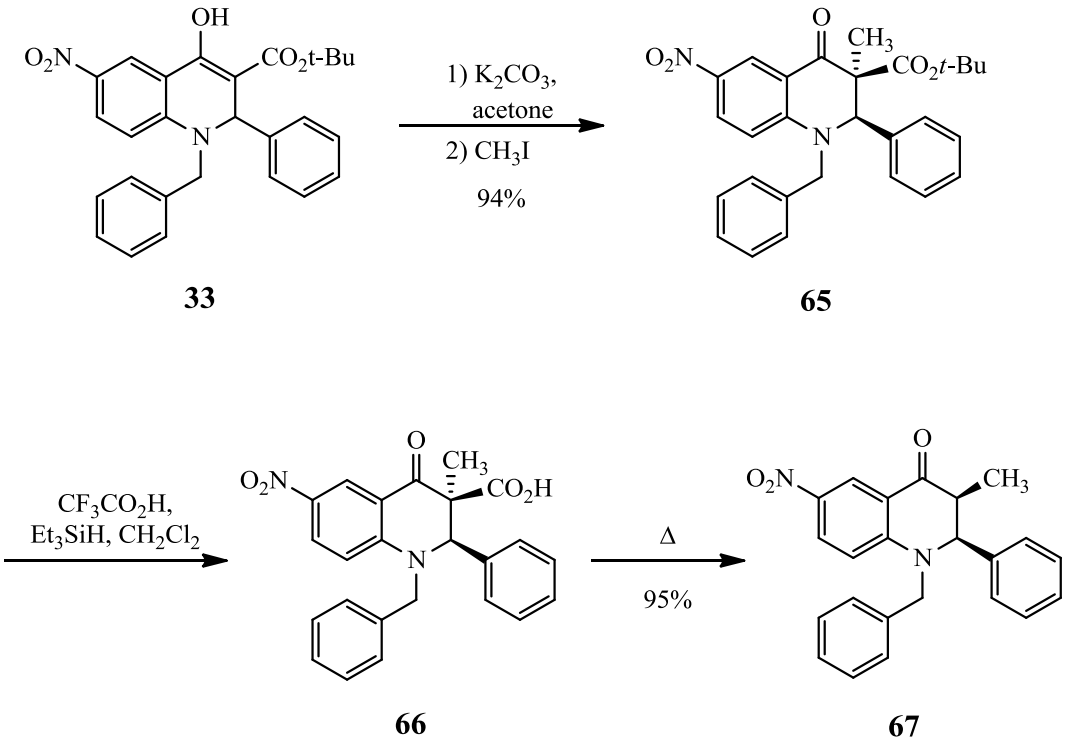
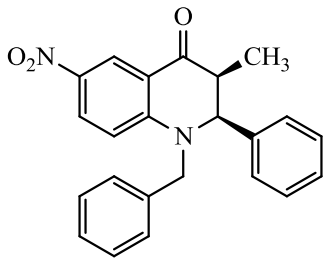


Figure 20. Alkylation and decarboxylation of 1,2,3,4-tetrahydroquinoline.



(±)-1-benzyl-3-methyl-6-nitro-2-phenyl-2,3-dihydroquinolin-4(1*H*)-one

67

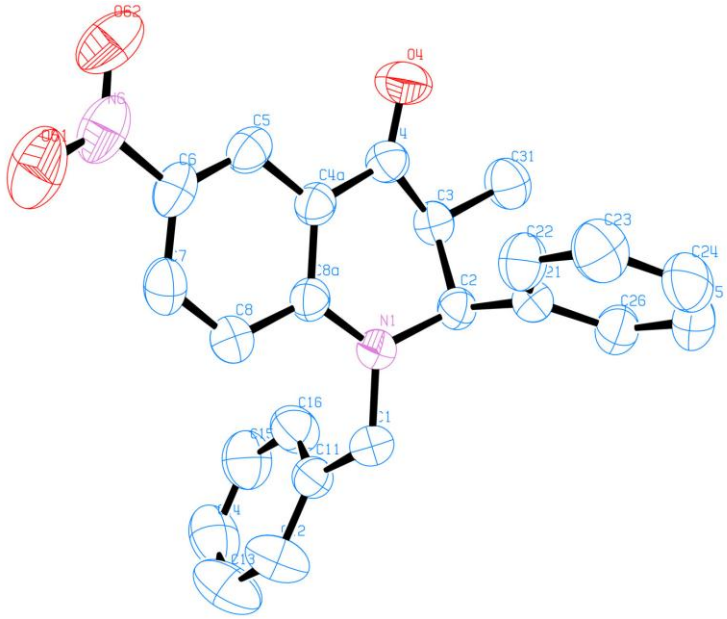
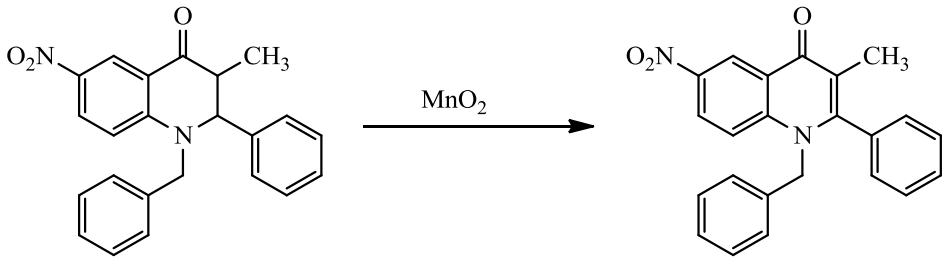


Figure 21. X-ray of **67**.

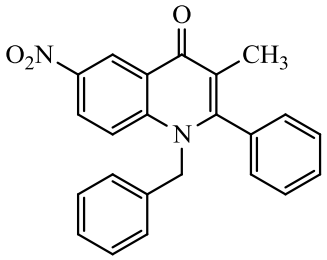
Synthesis of Tri-alkyl Subsituted 2,3-Dihydroquinolinone.

In an attempt to further derivatize the trisubstituted 1,2,3,4-tetrahydroquinolinone, **67** was converted to the corresponding 2,3-dihydroquinolinone **68** through a double bond migration reaction. Using the previous method for the synthesis of **64**, MnO_2 was used as the oxidizing agent to give the product **68** was isolated in a 51% yield after 3 days. An X-ray crystal structure was obtained to confirm the position of the double bond.



67 **68**

Figure 22. Synthesis of 2,3-dihydroquinolinone **68**.



1-benzyl-3-methyl-6-nitro-2-phenylquinolin-4(1*H*)-one

68

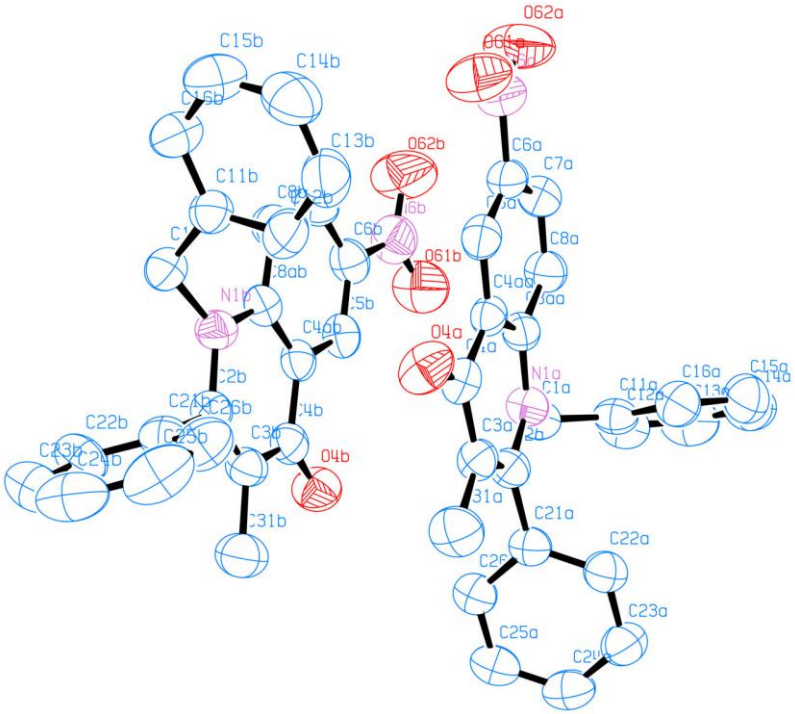


Figure 23. X-ray structure of **68**.

Conclusion

A new tandem imine addition-S_NAr reaction involving *in situ*-generated imines has been developed for the preparation of highly substituted 1,2,3,4-tetrahydroquinolinone-3-carboxlates in high yields. When using aromatic imines, the tandem imine addition-S_NAr reaction occurred spontaneously, without added base or catalyst. In the case of non-aromatic imines the tandem reaction was still spontaneous, but, the addition of molecular sieves was required to generate the aliphatic imines. Though imines of benzaldehyde derivatives and acetaldehyde proved effective in the tandem reaction, attempts to use ketones in the synthesis towards germinal substituted 1,2,3,4-tetrahydroquinolinone-3-carboxlates were unsuccessful.

The tandem imine addition-S_NAr reaction contains a number of desirable aspects. First, the tandem imine addition-S_NAr reaction is a very atom-economical reaction, using nearly every atom from the substrates in the final structure. Second, very few synthetic steps are required to achieve highly complex molecular structures. The use of tandem reactions minimizes the number workup steps and the amount of waste generated during the synthesis. Third, by incorporating the imine generation into the design of the tandem reaction, a large number of highly complex structures can be achieved in a limited number of steps.

To expand on the usefulness of the tandem imine addition-S_NAr reaction, the tandem products were converted to highly substituted 2,3-dihydroquinolinone and 1,2,3,4- tetrahydroquinolinones. The latter were accomplished by a double bond migration reaction and an alkylation-decarboxylation sequence, respectively. These

provide convenient methods towards similar known biologically active heterocyclic systems.[13-15]

Experimental

All reactions were run in dry glassware under N_2. The saturated NH_4Cl, saturated NaCl, 5% $NaHCO_3$, 5% Na_2SO_3 and 0.5 *M* HCl, used in work-up procedures refer to aqueous solutions. Liquid reagents were measured using a Socorex 10-100 µL autopipeter. Reactions were monitored by TLC on silica gel GF plates (Analtech No 21521).

Preparative separations were performed by one of the following methods: (1) flash column chromatography on silica gel (grade 62, 60–200 mesh) containing UV-active phosphor (Sorbent Technologies UV-05) packed into quartz columns or (2) P TLC on 20-cm × 20-cm silica gel GF plates (Analtech No 02015). Band elution for all chromatographic separations was monitored using a hand-held UV lamp. Melting points were uncorrected. IR spectra were run as thin films on NaCl disks. ^{1}H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ at 300 MHz and 75 MHz, respectively, using $(CH_3)_4Si$ as the internal standard; coupling constants (*J*) are given in Hz. Low resolution mass spectra (EI/DP) were obtained at 30 eV.

2-Fluoro-5-nitrobenzaldehyde (24).

To a 500 mL three-necked, round-bottomed flask 2-fluorobenzaldehyde **23** (14.5g, 117 mmol) was added dropwise using an addition funnel over 1 h to a solution of 11.0 g of $NaNO_3$ in 108.7 mL of concentrated H_2SO_4 at 0 ^{o}C: The reaction was stirred at 0 ^{o}C for 1.5 h and the solution was poured into a 1-L separatory funnel containing approximately 200 mL of ic, and was extracted twice with 200 mL portions of ether. (Caution should be

used during this workup as ether will evaporate rapidly causing increased pressure in the separatory funnel.) The combined ether layers were washed with water (2x), $NaHCO_3$ (1x), saturated NaCl (1x) and dried ($MgSO_4$). Filtration and removal of the solvent under vacuum gave a pale yellow solid. Recrystallization using minimal ether and hexanes yielded the desired product **24** (16.5g, 84%) as white needle-like crystals with a mp of 59 – 60 ^{o}C (lit.[46] 60 – 61 ^{o}C).

2-Fluoro-5-nitrobenzoic Acid (25).

2-Fluoro-5-nitrobenzaldehyde **24** (8.40 g, 53.2 mmol) was dissolved in 75 mL of acetone in a 500-mL round-bottomed flask. Fresh Jones reagent[33] (~3 mL) was added dropwise using an addition funnel over a 30 min period until a red-oragne color persisted. The reaction was stirred for an additional 1 h. An aqueous solution of 10% Na_2SO_3 was added to the reaction until the red-orange color dissipated. The solution was poured into a 1-L separatory flask containing about 200 mL of water and extracted twice with 200 mL portions of ether. The combined ether layers were washed with water (2x), saturated NaCl (1x) and dried ($MgSO_4$). Filtration and removal of the solvent under vacuum gave a pale white solid. Recrystallization from ether gave the product **25** (8.56 g, 93%) as a white crystalline solid, mp 140-142 ^{o}C (Aldrich Catalog 142-144 ^{o}C).

Representative Procedure for the β-Ketoesters: *tert*-Butyl 3-(2-Fluoro-5-nitro-phenyl)-3-oxopropanoate (28).

To a 250-mL round-bottomed flask 3.28 mL of $SOCl_2$ was added to a solution of 2-fluoro-5-nitrobenzoic acid **25** (4.76 g, 25.7 mmol) in 100 mL of benzene. The reaction was heated to reflux using an oil bath for 12 h and then concentrated under vacuum to give the acid chloride **26** as a clear oil that crystallized when stored in the freezer. This acid chloride was not characterized but was used directly in the next step.

In a dry 500-mL three necked, round-bottomed flask equipped with a magnetic stirrer, an, addition funnel and a rubber septum, *tert*-butyl hydrogen malonate (8.81 g, 55 mmol) and a catalytic amount of 2,2'-bipyridine were dissolved in 250 mL of freshly distilled tetrahydrofuran. The reaction vessel was cooled to -30^{o} C using a dry ice-acetone bath. At this temperature, one equivalent of *n*-butyllithium (55 mmol) was added dropwise using a syringe over a period of 30 min. Constant stirring was required to prevent a solid mass from forming. The reaction was warmed to -10 ^{o}C using a salt water ice bath. At this temperature, a second equivalent of *n*-butyllithium (55 mmol) was added dropwise using a syringe over 30 min until a red color persisted for 5 min.

The reaction was cooled to -78 ^{o}C using a dry ice-acetone bath. The acid chloride **26** was dissolved in 25 mL of freshly distilled THF, and the solution was added over a 30 min period to the reaction using an addition funnel. The reaction was stirred for 30 min at -78 ^{o}C and then an additional 30 min at -10 ^{o}C using a salt water-ice bath. The reaction was poured over approximately 200 mL of ice in a 1-L separatory funnel containing 3 equivalents of conc. HCl. The aqueous layer was extracted twice with 200 mL portions

of CH_2Cl_2, and the combined organic layers were washed with $NaHCO_3$ (1x), NH_4Cl (1x), saturated NaCl (1x), and dried over $MgSO_4$. The drying agent was filtered and the solvent was removed under vacuum to yield a red solid. Column chromatography using silica and 1% ether in hexanes yielded the enol of β-ketoester **28** (6.86g , 94%) as a white solid: mp 79-81 ^oC; IR: 1613, 1536, 1349 cm^{-1}; ^1H NMR: δ 12.9 (bs, 1H), 8.78 (dd, *J* = 6.6, 2.9 Hz, 1H), 8.29 (dt, *J* = 9.2, 3.5 Hz, 1H), 7.28 (t, *J* = 9.7 Hz, 1H), 5.81 (s, 1H), 1.55 (s, 9H); ^{13}C NMR: δ 172.7, 163.6 (d, *J* = 265.1 Hz), 162.8, 144.4, 127.0 (d, *J* = 11.2 Hz), 125.4 (d, *J* = 4.3 Hz), 117.6 (d, *J* = 14.6 Hz) 82.2, 28.2; MS: *m/z*.283 (M^+).

Anal. Calcd for $C_{13}H_{14}FNO_5$: C, 55.12; H, 4.98; N, 4.94. Found: C, 55.08; H, 4.99; N, 4.93.

Ethyl 3-(2-Fluoro-5-nitrophenyl)-3-oxopropanoate (29).

Ester **29** (6.51 g, 72%) was prepared as above from **25** (6.41 g, 35.4 mmol) isolated as a white solid; mp 60-61 ^oC; IR: 1645, 1622, 1493, 1350 cm^{-1}; ^1H NMR: δ 12.75 (s, 1H), 8.81 (dm, *J* = 4.9 Hz, 1H), 8.31 (dt, *J* = 9.3, 3.4 Hz, 1H), 7.30 (dd, *J* = 9.3, 9.3 Hz , 1H), 5.91 (s, 1H), 4.30 (q, *J* = 7.3 Hz, 2H), 1.36 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR: δ 172.8, 163.7 (*J* = 265.4 Hz), 163.2, 144.4, 127.3 (d, *J* = 11.2 Hz), 125.4 (d, *J* = 4.0 Hz), 117.7 (d, *J* = 25.8 Hz), 94.2 (d, *J* = 14.9 Hz), 61.0, 14.2; MS: *m/z*. 255 (M^+).

Anal. Calcd for $C_{11}H_{10}FNO_5$: C, 51.71; H, 3.95; N, 5.49. Found: C, 51.69; H, 3.92; N, 5.48.

Representative Procedure for the Tandum Imine Addition-S_NAr Reaction with β-Ketoesters and Aromatic Imines: *tert*-Butyl (±)-1-Benzyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (33).

In a 100-mL round-bottomed flask, benzylamine **31** (0.59 g, 5.50 mmol) and benzaldehyde **30** (0.63 g, 5.90 mmol) were stirred together in 3 mL of anhydrous DMF at room temperature for 6 h. Solid *tert*-butyl 3-(2-fluoro-5-nitro-phenyl)-3-oxopropanoate (**28**) (1.59 g, 5.6 mmol) was added directly to the reaction, resulting in an instantaneous color change from colorless to yellow. Stirring for an additional 6 h gave a yellow precipitate. The reaction was added to a 1-L separatory funnel containing 50 ml of water and extracted two portions of 15 mL CH_2Cl_2. The combined organic layers were washed with saturated NaCl (1x), dried over anhydrous $MgSO_4$, and concentrated under vacuum to give a yellow solid. Tritration with minimal ether afforded the desired product **33** (2.52 g, 90%) as a yellow powder; mp 163-165 ^oC; IR: 1655, 1634, 1504, 1321 cm^{-1}; ^1H NMR: δ 12.60 (s, 1H), 8.62 (d, *J* = 2.6 Hz, 1H), 7.98 (dd, *J* = 9.4, 2.6 Hz, 1H), 7.28 (m, 10H), 6.37 (d, *J* = 9.4 Hz, 1H), 5.45 (s, 1H), 4.51 (d, *J* = 16.9 Hz, 1H), 4.39 (d, *J* = 16.9 Hz, 1H), 1.36 (s 9H); ^{13}C NMR: δ 169.8, 160.3, 150.6, 142.0, 137.7, 135.2, 128.9, 128.6, 128.5, 128.4, 127.7, 126.9, 126.4, 121.9, 115.2, 110.9, 98.4, 82.9, 63.0, 52.3, 28.0; MS: *m/z.* 367 (M^+ -C_7H_7).

Anal. Calcd for $C_{27}H_{26}N_2O_5$: C, 70.73; H, 5.72; N, 6.11. Found: C, 70.89; H, 5.76; N, 6.08.

***tert*-Butyl (±)-1-Hexyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (34).**

Racemic ester **34** (122 mg, 93%) was prepared as above from **28** (82 mg, 0.30 mmol), hexylamine (307 mg, 0.30 mmol) and benzaldehyde (38 mg, 0.36 mmol) isolated yellow solid; mp 151-152 ^{o}C: IR: 1659, 1505, 1317 cm^{-1}; ^{1}H NMR: δ 12.50 (s, 1H), 8.59 (d, *J* = 2.9 Hz, 1H), 8.10 (dd, *J* = 9.3, 2.9 Hz, 1H), 7.26 (s, 5H), 6.43 (d, *J* = 9.3 Hz, 1H), 5.36 (s, 1H), 3.21 (complex, 2H), 1.41 (s, 9H), 1.27 (m, 8H), 0.86 (complex, 3H); ^{13}C NMR: δ 169.7, 160.2, 150.2, 142.7, 136.8, 128.7, 128.4, 128.3, 126.8, 122.0, 114.4, 109.8, 98.0, 82.7, 63.2, 49.5, 31.3, 28.0, 26.4, 26.2, 22.4, 13.9; MS: *m/z* 381 (M^{+}-C_5H_{11}).

Anal. Calcd for $C_{26}H_{32}N_2O_5$: C, 69.01; H, 6.19; N, 6.19. Found: C, 69.07; H, 6.13; N, 6.14.

***tert*-Butyl (±)-1-Isobutyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (35).**

Racemic ester **35** (407 mg, 95%) was prepared as above from **28** (285 mg, 1.01 mmol), isobutylamine (74 mg, 1.01 mmol) and benzaldehyde (128 mg, 1.20 mmol) isolated as a yellow solid; mp 134-135 ^{o}C: IR: 1721, 1652, 1506, 1321, 1259 cm^{-1}; ^{1}H NMR: δ 12.48 (s, 1H), 8.57 (d, *J* = 2.6 Hz, 1H), 8.08 (dd, *J* = 9.4, 3.0 Hz, 1H), 7.26 (s, 5H), 6.47 (d, *J* = 9.4 Hz , 1H), 5.36 (s 1H), 3.29 (dd, *J* = 14.5, 5.1 Hz, 1H), 2.79 (dd, *J* = 14.5, 9.4 Hz, 1H), 2.10 (m, 1H), 1.43 (s, 9H), 1.06 (d, *J* = 6.8 Hz, 3H), 0.94 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR: δ 169.7, 160.5, 150.9, 142.1, 128.6, 128.5, 128.3, 126.7, 122.3, 115.1, 110.4, 98.1, 82.8, 56.2, 28.2, 26.3, 20.11, 20.10; MS: *m/z* 385 (M^{+} -C_3H_7).

Anal. Calcd for $C_{24}H_{28}N_2O_5$: C, 67.91; H, 6.65; N, 6.60. Found: C, 68.01; H, 6.58; N, 6.64.

tert-Butyl (±)-1-Cyclopropyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (36).

Racemic ester **36** (57 mg, 79%) was prepared as above from **28** (50 mg, 0.177 mmol), cyclopropylamine (10 mg, 0.177 mmol) and benzaldehyde (23 mg, 0.21 mmol) isolated as a yellow solid; mp 175-176 ^{o}C: IR: 1655, 1494, 1322, 1291 cm^{-1}; ^{1}H NMR: δ 12.5 (s, 1H), 8.6 (d, *J* = 2.4 Hz, 1H), 8.11 (dd, *J* = 9.4, 2.4 Hz, 1H), 7.26 (s, 5H), 6.94 (d, *J* = 9.3 Hz, 1H), 5.37 (s, 1H), 2.18 (m, 1H), 1.38 (s, 9H), 0.97 (m, 4H); ^{13}C NMR: δ 160.3, 151.7, 140.8, 138.5, 129.9, 128.4, 128.2, 128.0, 126.8, 121.3, 116.4, 112.7, 99.2, 82.6, 61.6, 29.8, 28.1, 10.9, 7.9; MS: *m/z* 408 (M^+).

Anal. Calcd for $C_{23}H_{24}N_2O_5$: C, 67.63; H, 5.92; N, 6.86. Found: C, 67.60; H, 6.00; N, 6.85.

tert-Butyl (±)-1-Allyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (37).

Racemic ester **37** (54 mg, 75%) was prepared as above from **28** (50 mg, 0.177 mmol), allylamine (10 mg, 1.00 mmol) and benzaldehyde (23 mg, 0.21 mmol) isolated as a yellow solid; mp 155-156 ^{o}C: IR: 1728, 1656, 1504, 1320, 1255 cm^{-1}; ^{1}H NMR: δ 12.56 (s, 1H), 8.59 (d, *J* = 2.4 Hz, 1H), 8.07 (dd, *J* = 9.3, 2.4 Hz, 1H), 7.27 (s, 5H), 6.45 (d, *J* =

9.3 Hz, 1H), 5.57 (complex, 1H), 5.38 (s, 1H), 5.18 (m, 2H), 3.93 (dd, *J* = 17.1, 4.8 Hz, 1H), 3.83 (dd, *J* = 17.1, 4.8 Hz , 1H), 1.39 (s, 9H); ^{13}C NMR: δ 169.7, 160.2, 150.3, 142.3, 137.5, 131.3, 128.6, 128.5, 128.4, 127.0, 121.9, 117.8, 114.7, 110.5, 98.2, 82.8, 63.0, 51.7, 28.1; MS: *m/z* 367 (M^+-C_3H_5).

Anal. Calcd for $C_{23}H_{24}N_2O_5$: C, 67.63; H, 5.92; N, 6.86. Found: C, 67.61; H, 6.03; N, 6.83.

Ethyl (±)-1-Benzyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (38).

Racemic ester **38** (383 mg, 89%) was prepared as above from **29** (255 mg, 1.0 mmol), benzylamine (107 mg, 1.00 mmol) and benzaldehyde (127 mg, 1.20 mmol) isolated as a yellow solid; mp 160-162 ^{o}C: IR: 1657, 1632, 1504, 1317, 1255 cm^{-1}; ^{1}H NMR: δ 12.57 (s, 1H), 8.81 (d, *J* = 2.7 Hz, 1H), 8.19 (dd, *J* = 9.2, 2.7 Hz, 1H), 7.46 (m, 10H), 6.60 (d, *J* = 9.2 Hz, 1H), 5.71 (s, 1H) 4.72 (d, *J* = 16.9 Hz, 1H), 4.54 (d, *J* = 16.9 Hz, 1H), 4.34 (m, 2H), 1.37 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR: δ 169.9, 160.7, 150.7, 137.8, 135.1, 129.0, 128.8, 128.6, 128.5, 127.8, 126.8, 126.3, 122.2, 114.9, 110.9, 97.2, 62.6, 61.1, 52.3, 13.9; MS: *m/z* 339 (M^+-C_7H_7).

Anal. Calcd for $C_{25}H_{22}N_2O_5$: C, 69.76; H, 5.15; N, 6.51. Found: C, 69.71; H, 5.13; N, 6.48.

Ethyl (±)-1-Hexyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (39).

Racemic ester **39** (415 mg, 98%) was prepared as above from **29** (255 mg, 1.00 mmol), hexylamine (99 mg, 1.00 mmol) and benzaldehyde (128 mg, 1.20 mmol) isolated as a yellow solid; mp 141-142 ^{o}C: IR: 1659, 1633, 1505, 1315 cm^{-1}; ^{1}H NMR: δ 12.30 (s, 1H), 8.58 (d, *J* = 2.8 Hz, 1H), 8.11 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.27 (s, 5H), 6.47 (d, *J* = 9.2 Hz, 1H), 5.46 (s, 1H), 4.19 (q, *J* = 7.3 Hz, 2H), 3.30 (m, 1H), 3.17 (m, 1H), 1.61 (m, 2H), 1.25 (m, 9H), 0.88 (complex, 3H); ^{13}C NMR: δ 169.8, 160.6, 150.4, 142.6, 137.0, 128.9, 128.6, 128.3, 126.4, 122.3, 114.3, 109.9, 96.9.0, 62.7, 61.0, 49.7, 31.3, 26.5, 26.4, 22.5, 14.0, 13.9; MS: *m/z* 353 (M^{+}-C_5H_{11}).

Anal. Calcd for $C_{24}H_{28}N_2O_5$: C, 67.91; H, 6.65; N, 6.60. Found: C, 68.07; H, 6.53; N, 6.54.

Ethyl (±)-1-Isobutyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (40).

Racemic ester **40** (284 mg, 72%) was prepared as above from **29** (255 mg, 1.00 mmol), isobutylamine (73 mg, 1.00 mmol) and benzaldehyde (127 mg, 1.20 mmol) isolated as a yellow solid; mp 136-138 ^{o}C: IR: 1657, 1632, 1504, 1315, 1254 cm^{-1}; ^{1}H NMR: δ 12.28 (s, 1H), 8.58 (d, *J* = 2.9 Hz, 1H), 8.10 (dd, *J* = 9.3, 2.9 Hz, 1H), 7.26 (s, 5H), 6.52 (d, *J* = 9.3 Hz, 1H) 5.46 (s, 1H), 4.22 (m, 2H), 3.32 (dd, *J* = 14.6, 5.4 Hz, 1H), 2.80 (dd, *J* = 14.6, 9.3 Hz, 1H), 2.14 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.07 (d, *J* = 6.3 Hz. 3H), 0.94 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR: δ 169.8, 160.8, 151.0, 141.9, 137.1, 128.7, 128.5, 128.3,

126.5, 122.3, 114.7, 110.5, 96.9, 62.9, 61.0, 56.3, 26.3, 20.0, 19.9, 13.9; MS: *m/z* 385 (M^+-C_3H_7).

Anal. Calcd for $C_{22}H_{24}N_2O_5$: C, 66.65; H, 6.10; N, 7.07. Found: C, 66.60; H, 6.05; N, 7.04.

Ethyl (±)-1-Cyclopropyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (41).

Racemic ester **41** (324 mg, 85%) was prepared as above from **29** (255 mg, 1.00 mmol), cyclopropylamine (57 mg, 1.00 mmol) and benzaldehyde (127 mg, 1.20 mmol) isolated as a yellow solid; mp 184-186 ^oC: IR: 1658, 1633, 1494, 1320 cm^{-1}; ^1H NMR: δ 12.30 (s, 1H), 8.58 (d, *J* = 2.4 Hz, 1H), 8.13 (dd, *J* = 9.3, 2.4 Hz, 1H), 7.23 (s, 5H), 6.98 (d, *J* = 9.3 Hz, 1H), 5.46 (s, 1H), 4.18 (q, *J* = 7.1 Hz , 2H), 2.21 (complex, 1H), 1.22 (t, *J* = 7.1 Hz, 3H), 0.95 (m, 4H); ^{13}C NMR: δ 169.9, 160.7, 151.8, 140.6, 138.5, 128.5, 128.3, 128.1 126.6, 121.4, 116.1, 112.8, 97.9, 61.2, 29.9, 14.0, 10.8, 7.9; MS: *m/z* 380 (M^+).

Anal. Calcd for $C_{21}H_{20}N_2O_5$: C, 66.31; H, 5.30; N, 7.36; Found: C, 66.40; H, 5.24; N, 7.30.

Ethyl (±)-1-Allyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (42).

Racemic ester **42** (368 mg, 97%) was prepared as above from **29** (255 mg, 1.00 mmol), allylamine (57 mg, 1.00 mmol) and benzaldehyde (127 mg, 1.20 mmol) isolated as a

yellow solid; mp 179-180 ^{o}C: IR: 1653, 1629, 1504, 1309, 1256 cm^{-1}; ^{1}H NMR: δ 12.35 (s, 1H), 8.60 (d, *J* = 2.4 Hz, 1H), 8.09 (dd, *J* = 9.3, 2.4 Hz, 1H), 7.27 (s, 5H), 6.48 (d, *J* = 9.3 Hz, 1H), 5.60 (ddt, *J* = 17.1, 10.3, 5.4 Hz, 1H), 5.47 (s, 1H), 5.21 (d, *J* = 17.1 Hz, 1H), 5.20 (d, *J* = 10.3, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.95 (dd, *J* = 17.1, 5.4 Hz, 1H), 3.81 (dd, *J* = 17.1, 5.4 Hz , 1H), 1.23 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR: δ 169.9, 160.5, 150.5, 142.1, 137.6, 131.2, 128.8, 128.6, 128.5, 126.9, 122.1, 117.9, 114.5, 110.6, 97.1, 62.5, 61.1, 51.7, 14.0; MS: *m/z* 380 (M^{+}).

Anal. Calcd for $C_{21}H_{20}N_2O_5$: C, 66.31; H, 5.30; N, 7.36; Found: C, 66.40; H, 5.24; N, 7.30.

tert-Butyl (±)-1-Benzyl-2-(4-methoxyphenyl)-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (43).

Racemic ester **43** (96 mg, 82%) was prepared as above from **28** (68 mg, 0.24 mmol), benzylamine (26 mg, 0.24 mmol) and 4-methoxybenzaldehyde (39 mg, 0.29 mmol) isolated as a yellow solid; mp 161-164 ^{o}C: IR: 2838, 1655, 1633, 1510, 1320 cm^{-1}; ^{1}H NMR: δ 12.56 (s, 1H), 8.61 (d, *J* = 2.6 Hz, 1H), 7.98 (dd, *J* = 9.4, 2.6 Hz, 1H), 7.26 (m, 7H), 6.8 (d, *J* = 8.5 Hz, 2H), 6.36 (d, *J* = 9.4 Hz, 1H), 5.39 (s, 1H), 4.49 (d, *J* = 16.9 Hz, 1H), 4.39 (d, *J* = 16.9 Hz, 1H), 3.78 (s, 3H), 1.37 (s, 9H); ^{13}C NMR: δ 169.8, 160.1, 159.6, 150.5, 137.7, 135.3, 134.4, 128.9, 128.6, 128.2, 127.7, 126.4, 121.9, 115.1, 113.8, 110.9, 98.6, 82.8, 62.3, 55.3, 53.2, 28.1; MS: *m/z* 397 (M^{+}-C_7H_7).

Anal. Calcd for $C_{28}H_{28}N_2O_6$: C, 68.84; H, 5.78; N, 5.73; Found: C, 68.70; H, 5.74; N, 5.69.

***tert*-Butyl (±)-1-Benzyl-2-(4-fluorophenyl)-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (44).**

Racemic ester **44** (171 mg 97%) was prepared as above from **28** (105 mg, 0.37 mmol), benzylamine (26 mg, 0.37 mmol) and 4-fluorobenzaldehyde (55 mg, 0.44 mmol) isolated as a yellow solid; mp 165-166 ^{o}C: IR: 1655, 1602, 1506, 1321cm^{-1}; ^{1}H NMR: δ 12.58 (s, 1H), 8.63 (d, *J* = 2.6 Hz, 1H), 8.00 (dd, *J* = 9.4, 2.6 Hz, 1H), 7.26 (m, 8H), 6.97 (t, *J* = 8.5 Hz, 1H), 6.39 (d, *J* = 9.4 Hz, 1H), 5.43 (s, 1H), 4.51 (d, *J* = 17.1 Hz, 1H), 4.37 (d, *J* = 17.1 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR: δ 169.9, 162.7 (d, *J*= 245.0 Hz) 160.4, 150.4, 142.0, 138.0, 135.1, 129.0, 128.6 (d, *J* = 7.7 Hz), 127.8, 127.0, 126.4, 122.0, 115.2 (d, *J* = 16.6 Hz), 115.1, 111.0, 98.3, 83.0, 62.2, 52.4, 28.1; MS: *m/z* 385 (M^{+}-C_7H_7).

Anal. Calcd for $C_{27}H_{25}FN_2O_5$: C, 68.06; H, 5.29; N, 5.88; Found: C, 68.07; H, 5.27; N, 5.79.

***tert*-Butyl (±)-1-Benzyl-2-(4-trifluoromethylphenyl)-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (45).**

Racemic ester **45** (200 mg, 92%) was prepared as above from **28** (117 mg, 0.41 mmol), benzylamine (44 mg, 0.41 mmol) of and 4-trifluoromethylbenzaldehyde (86 mg, 0.50 mmol) isolated as a yellow solid; mp 161-163 ^{o}C: IR: 1659, 1506, 1407, 1321 cm^{-1}; ^{1}H NMR: δ 12.62 (s, 1H), 8.63 (d, *J* = 2.4 Hz, 1H), 8.01 (dd, *J* = 9.3, 2.4 Hz, 1H), 7.55 (d, *J* = 7.8 Hz, 2H), 7.39 (d, *J* = 7.8 Hz, 2H), 7.26 (m, 5H), 6.44 (d, *J* = 9.3 Hz, 1H), 5.53 (s, 1H), 4.55 (d, *J* = 17.1 Hz, 1H), 4.36 (d, *J* = 17.1 Hz, 1H), 1.38 (s, 9H); ^{13}C NMR: δ 169.4, 160.7, 150.4, 145.7, 138.1, 134.5, 130.6 (q, *J* = 32.6 Hz) 129.0, 128.8, 127.9,

127.2, 126.4, 125.6, 123.7 (q, *J* = 260 Hz), 122.0, 115.1, 111.1, 97.8, 83.3, 62.4, 52.7, 28.1; MS: *m/z* 435 (M^+-C_7H_7).

Anal. Calcd for $C_{28}H_{25}F_3N_2O_5$: C, 63.87; H, 4.79; N, 5.32; Found: C, 63.67; H, 4.65; N, 5.25.

Ethyl (±)-1-Benzyl-2-(4-methoxyphenyl)-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (46).

Racemic ester **46** (336 mg, 73%) was prepared as above from **29** (255 mg, 1.00 mmol), benzylamine (107 mg, 1.00 mmol) and 4-methoxybenzaldehyde (163 mg, 1.20 mmol) isolated as a yellow solid; mp 120-121 ^oC: IR: 2838, 1658, 1510, 1317, 1255 cm^{-1}; ^1H NMR: δ 12.36 (s, 1H), 8.62 (d, *J* = 2.7 Hz, 1H), 8.00 (dd, *J* = 9.3, 2.7 Hz, 1H), 7.25 (m, 7H), 6.80 (d, *J* = 8.7 Hz, 2H), 6.40 (d, *J* = 9.3 Hz, 1H), 5.48 (s, 1H), 4.53 (d, *J* = 16.9 Hz, 1H), 4.37 (d, *J* = 16.9 Hz, 1H), 4.16 (m, 2H), 3,78 (s, 3H), 1.19 (m, 3H); ^{13}C NMR: δ 169.9, 160.4, 159.7, 150.6, 137.7, 135.2, 134.2, 129.0, 128.8, 128.0, 127.7, 126.3, 122.1, 114.8, 113.9, 110.9, 97.4, 65.8, 61.9, 55.2, 52.1, 13.9; MS: *m/z* 369 (M^+-C_7H_7).

Anal. Calcd for $C_{26}H_{24}N_2O_6$: C, 68.84; H, 5.78; N, 5.73; Found: C, 68.70; H, 5.74; N, 5.69.

Ethyl (±)-1-Benzyl-2-(4-fluorophenyl)-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (47).

Racemic ester **47** (413 mg, 92%) was prepared as above from **29** (255 mg, 1.00 mmol), benzylamine (107 mg, 1.00 mmol) and 4-fluorobenzaldehyde (149 mg, 1.20 mmol) isolated as a yellow solid; mp 134-135 ^{o}C: IR: 1660, 1633, 1602, 1506, 1317, 1255 cm^{-1}; ^{1}H NMR: δ 12.38 (s, 1H), 8.63 (d, *J* = 2.4 Hz, 1H), 8.02 (dd, *J* = 9.3, 2.4 Hz, 1H), 7.26 (m, 7H), 6.97 (t, *J* = 8.5 Hz, 2H), 6.43 (d, *J* = 9.3 Hz, 1H), 5.53 (s, 1H), 4.55 (d, *J* = 16.6 Hz, 1H), 4.35 (d, *J* = 16.6 Hz, 1H), 4.17 (m, 2H), 1.19 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR: δ 169.7, 162.6 (d, *J* = 247.3), 160.6, 150.5, 137.9 (d, *J* = 5.7 Hz), 135.0, 129.1, 128.9, 128.5 (d, *J* = 8.0 Hz), 127.8, 126.4, 122.2, 115.6 (d, *J* = 21.5 Hz), 114.8, 111.0, 97.1, 61.8, 52.3, 13.9; MS: *m/z* 357 (M^{+}-C_7H_7).

Anal. Calcd for $C_{25}H_{21}FN_2O_5$: C, 66.96; H, 4.72; N, 6.25; Found: C, 66.87; H, 4.65; N, 6.21.

Ethyl (±)-1-Benzyl-2-(4-trifluoromethyphenyl)-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (48).

Racemic ester **48** (273 mg, 55%) was prepared as above from **29** (255 mg, 1.00 mmol), benzylamine (107 mg, 1.00 mmol) and 4-trifluoromethylbenzaldehyde (209 mg, 1.20 mmol) isolated as a yellow solid; mp 165-166 ^{o}C: IR: 1660, 1633, 1504, 1317 cm^{-1}; ^{1}H NMR: δ 12.42 (s, 1H), 8.64 (d, *J* = 2.9 Hz, 1H), 8.03 (dd, *J* = 9.3, 2.9 Hz, 1H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 2H), 7.32 (m, 3H), 7.21 (d, *J* = 6.3 Hz, 2H), 6.48 (d, *J* = 9.3 Hz, 1H), 5.63 (s, 1H), 4.59 (d, *J* = 16.6 HZ, 1H), 4.34 (d, *J* = 16.6 HZ, 1H), 4.18 (q,

J = 7.1 HZ, 2H), 1.21 (t, *J* = 7.1 HZ, 3H); ^{13}C NMR: δ 169.6, 161.0, 150.5, 145.5, 138.1, 134.8, 130.6 (q, *J* = 32.6 Hz), 129.0, 128.9, 127.9, 127.1, 126.4, 125.7 (q, *J* = 3.7 Hz), 123.8 (q, *J* = 272.3 Hz), 122.2, 114.8, 111.2, 96.6, 62.0, 61.3, 52.6, 13.9; MS: *m/z* 407 (M^+-C_7H_7).

Anal. Calcd for $C_{26}H_{21}F_3N_2O_5$: C, 62.65; H, 4.25; N, 5.62; Found: C, 62.67; H, 4.15; N, 5.55.

Representative Procedure for the Tandum Imine Addition-S_NAr Reaction with β-Ketoesters and Aliphatic Imines: *tert*-Butyl (±)-1-Benzyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (51).

In a 100-mL round-bottomed flask, benzylamine (**31**) (37 mg, 0.35 mmol) and acetaldehyde (**49**) (20 mg, 0.44 mmol) were stirred together with *ca.* 25 mg of 4 Å molecular sieves in 3 mL of DMF at room temperature for 6 h. *tert*-Butyl 3-(2-fluoro-5-nitro-phenyl)-3-oxopropanoate (**28**) (100mg, 0.35 mmol) was added directly as the solid and stirred for 5 min to give a yellow to red solution. The molecular sieves were filtered from the reaction through a pad of Celite®, and the filtrate was added to a separatory funnel containing 50 mL of water and extracted twice with CH_2Cl_2. The combined organic layers were washed with saturated NaCl (1x), dried ($MgSO_4$) and concentrated under vacuum to give a yellow solid. Purification by column chromatography over silica using 5-10% ether in hexanes afforded the desired product (**51**) (128 mg, 92%) as a yellow solid; mp 145-147 ^oC: IR: 1655, 1505, 1317 cm^{-1}; ^{1}H NMR: δ 12.36 (s, 1H), 8.54 (d, *J* = 2.4 Hz, 1H), 7.98 (dd, *J* = 9.3, 2.4 Hz, 1H), 7.31 (m, 5H), 6.41 (d, *J* = 9.3 Hz, 1H),

4.71 (d, *J* = 16.6 Hz, 1H), 4.56 (d, *J* = 16.6 Hz, 1H), 4.52 (q, *J* = 5.9 Hz, 1H), 1.52 (s, 9H), 1.26 (d, *J* = 5.9 Hz, 3H); ^{13}C NMR: δ 169.6, 160.5, 150.3, 137.6, 135.7, 128.9, 128.0, 127.7, 126.4, 121.7, 115.7, 111.8, 99.1, 82.4, 55.0, 53.3, 28.2, 20.6; MS: *m/z* 305 (M^+-C_7H_7).

Anal. Calcd for $C_{22}H_{24}N_2O_5$: C, 66.65; H, 6.10; N, 7.07; Found: C, 66.67; H, 6.15; N, 7.05.

***tert*-Butyl (±)-1-Hexyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (52).**

Racemic ester **52** (186 mg, 97%) was prepared as above from **28** (140 mg, 0.50 mmol), hexylamine (50 mg, 0.50 mmol) and acetaldehyde (27 mg, 0.60 mmol) isolated as a yellow solid; mp 86-87 ^{o}C: IR: 1656, 1505, 1316 cm^{-1}; ^{1}H NMR: δ 12.28 (s, 1H), 8.50 (d, *J* = 2.9 Hz , 1H), 8.08 (dd, *J* = 9.3, 2.9 Hz, 1H), 6.49 (d, *J* = 9.3 Hz, 1H), 4.43 (q, *J* = 6.4 Hz, 1H), 3.53 (complex, 1H), 3.23 (complex, 1H), 1.66 (m, 2H), 1.56 (s, 9H), 1.35 (m, 6H), 1.21 (d, *J* = 6.4 Hz, 3H), 0.91 (m 3H); ^{13}C NMR: δ 169.6, 160.6, 150.1, 136.9, 128.2, 122.0, 115.2, 110.7, 98.6, 82.3, 54.6, 49.6, 31.4, 28.3, 27.3, 26.5, 22.6, 20.8, 13.9; MS: *m/z* 319 (M^+-C_5H_{11}).

Anal. Calcd for $C_{21}H_{30}N_2O_5$: C, 64.59; H, 7.74; N, 7.17; Found: C, 64.67; H, 7.53; N, 7.05.

***tert*-Butyl (±)-1-Isobutyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (53).**

Racemic ester **53** (144 mg, 81%) was prepared as above from **28** (140 mg, 0.50 mmol), isobutylamine (37 mg, 0.50 mmol) and acetaldehyde (26 mg, 0.60 mmol) isolated as a yellow solid; mp 135-136 ^{o}C: IR: 1651, 1602, 1505, 1317 cm^{-1}; ^{1}H NMR: δ 12.26 (s, 1H), 8.52 (d, *J* = 2.9 Hz, 1H), 8.07 (dd, *J* = 9.3, 2.9 Hz, 1H), 6.50 (d, *J* = 9.3 Hz, 1H), 4.38 (q, *J* = 6.4 Hz, 1H), 3.54 (dd, *J* = 14.4, 5.1 Hz, 1H), 2.85 (dd, *J* = 14.4, 9.5 Hz, 1H), 2.03 (complex, 1H), 1.55 (s, 9H), 1.18 (d, *J* = 6.4 Hz, 3H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR: δ 169.6, 160.8, 150.4, 136.9, 128.1, 122.1, 115.4, 111.1, 98.6, 82.3, 56.6, 55.1, 28.3, 26.7, 20.1, 19.9; MS: *m/z* 319 (M^{+}-C_3H_7).

Anal. Calcd for $C_{19}H_{26}N_2O_5$: C, 62.97; H, 7.23; N, 7.73; Found: C, 62.77; H, 7.30; N, 7.65.

***tert*-Butyl (±)-1-Cyclopropyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (54).**

Racemic ester **54** (260 mg, 75%) was prepared as above from **28** (283 mg, 1.00 mmol), cyclopropylamine (57 mg, 1.00 mmol) of and acetaldehyde (53 mg, 1.20 mmol) isolated as a yellow solid; mp 142-143 ^{o}C: IR: 1654, 1507, 1322 cm^{-1}; ^{1}H NMR: δ 12.26 (s, 1H), 8.49 (d, *J* = 2.4 Hz, 1H), 8.13 (dd, *J* = 9.3, 2.4 Hz, 1H), 7.02 (d, *J* = 9.3 Hz, 1H), 4.48 (q, *J* = 6.4 Hz, 1H), 2.62 (m, 1H), 1.56 (s, 9H), 1.24 (d, *J* = 6.4 Hz, 3H), 1.09 (m, 1H), 0.97 (m, 1H), 0.78 (m, 1H), 0.64 (m, 1H); ^{13}C NMR: δ 169.6, 160.2, 151.9, 138.4, 127,7, 121.2, 116.5, 113.0, 100.2, 82.3, 53.3, 29.4, 28.3, 18.8, 10.5, 7.5; MS: *m/z* 346 (M^{+}).

Anal. Calcd for $C_{18}H_{22}N_2O_5$: C, 62.42; H, 6.40; N, 8.09; Found: C, 62.40; H, 6.50; N, 8.10.

tert-Butyl (±)-1-Allyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (55).

Racemic ester **55** (226 mg, 65%) was prepared as above from **28** (283 mg, 1.00 mmol), allylamine (57 mg, 1.00 mmol)and acetaldehyde (53 mg, 1.00 mmol) isolated as a yellow solid; mp 99-100 ^{o}C: IR: 1656, 1631, 1505, 1321 cm^{-1}; ^{1}H NMR: δ 12.31 (s, 1H), 8.52 (d, *J* = 2.4 Hz, 1H), 8.07 (dd, *J* = 9.3, 2.4 Hz, 1H), 6.50 (d, *J* = 9.3 Hz, 1H), 5.87 (m, 1H), 5.30 (d, *J* = 17.6 Hz, 1H), 5.29 (d, *J* = 9.8 Hz, 1H), 4.47 (q, *J* = 6.4 Hz, 1H), 4.09 (dd, *J* = 17.1, 4.9 Hz, 1H), 3.97 (dd, *J* = 17.1, 4.9 Hz, 1H), 1.55 (s, 9H), 1.23 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR: δ 169.6, 160.3, 150.2, 137.2, 132.2, 128.0, 121.6, 117.7, 115.2, 111.3, 98.9, 82.4, 54.8, 52.4, 28.2, 27.8; MS: *m/z* 346 (M^+).

Anal. Calcd for $C_{18}H_{22}N_2O_5$: C, 62.42; H, 6.40; N, 8.09; Found: C, 62.47; H, 6.53; N, 8.05.

Ethyl (±)-1-Benzyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (56).

Racemic ester **56** (352 mg, 96%) was prepared as above from **29** (255 mg, 1.00 mmol), benzylamine (107 mg, 1.00 mmol) and acetaldehyde (53 mg, 1.20 mmol) isolated as a yellow solid; mp 157-159 ^{o}C: IR: 1660, 1631, 1507, 1316 cm^{-1}; ^{1}H NMR: δ 12.21 (s,

1H), 8.54 (d, *J* = 2.4 Hz, 1H), 7.97 (dd, *J* = 9.3, 2.4 Hz, 1H), 7.30 (m, 5H), 6.44 (d, *J* = 9.3 Hz, 1H), 4.73 (d, *J* = 17.1 Hz, 1H), 4.63 (q, *J* = 6.4 Hz, 1H), 4.57 (d, *J* = 17.1 Hz, 1H), 4.29 (m, 2H), 1.30 (m, 6H); ^{13}C NMR: δ 169.8, 161.0, 150.3, 137.6, 135.7, 128.9, 128.2, 127.7, 126.4, 121.9, 115.4, 111.9, 97.8, 60.9, 54.7, 53.2, 20.7, 14.1; MS: *m/z* 277 (M^+-C_7H_7).

Anal. Calcd for $C_{20}H_{20}N_2O_5$: C, 65.21; H, 5.47; N, 7.60; Found: C, 65.17; H, 5.35; N, 7.55.

Ethyl (±)-1-Hexyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (57).

Racemic ester **57** (339 mg, 94%) was prepared as above from **29** (255 mg, 1.00 mmol), hexylamine (99 mg, 1.00 mmol) and acetaldehyde (53 mg, 1.20 mmol) isolated as a yellow solid; mp 78-80 ^{o}C: IR: 1658, 1631, 1505, 1312 cm^{-1}; ^{1}H NMR: δ 12.11 (s, 1H), 8.51 (d, *J* = 2.8 Hz , 1H), 8.09 (dd, *J* = 9.2, 2.8 Hz, 1H), 6.51 (d, *J* = 9.2 Hz, 1H), 4.52 (q, *J* = 6.0 Hz, 1H), 4.31 (m, 2H), 3.55 (dt, *J* = 7.3, 6.9 Hz, 1H), 3.22 (dt, *J* = 7.8, 6.9 Hz, 1H), 1.68 (m, 2H), 1.36 (m, 9H), 1.23 (d, *J* = 6.0 Hz, 3H), 0.90 (m 3H); ^{13}C NMR: δ 169.8, 161.2, 150.2, 137.0, 128.4, 122.3, 115.0, 110.8, 97.4, 60.9, 54.2, 49.7, 31.4, 28.3, 27.4, 26.5, 22.5, 20.9, 14.3, 13.9; MS: *m/z* 319 (M^+-C_5H_{11}).

Anal. Calcd for $C_{19}H_{26}N_2O_5$: C, 62.97; H, 7.23; N, 7.73; Found: C, 62.67; H, 7.13; N, 7.65.

Ethyl (±)-1-Isobutyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (58).

Racemic ester **58** (297 mg, 89%) was prepared as above from **29** (255 mg, 1.00 mmol), isobutylamine (73 mg, 1.00 mmol) and acetaldehyde (53 mg, 1.20 mmol) isolated as a yellow solid; mp 139-140^{o}C: IR: 1657, 1630, 1505, 1311 cm^{-1}; ^{1}H NMR: δ 12.10 (s, 1H), 8.53 (d, *J* = 2.8 Hz, 1H), 8.08 (dd, *J* = 9.2, 2.8 Hz, 1H), 6.51 (d, *J* = 9.2 Hz, 1H), 4.47 (q, *J* = 6.0 Hz, 1H), 4.31 (m, 2H), 3.54 (dd, *J* = 14.4, 5.3 Hz, 1H), 2.86 (dd, *J* = 14.4, 9.4 Hz, 1H), 2.05 (complex, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.20 (d, *J* = 6.0 Hz, 3H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR: δ 169.8, 161.3, 150.4, 137.0, 128.2, 122.3, 115.1, 111.2, 97.3, 60.9, 56.6, 54.7, 26.7, 20.1, 19.9, 19.8, 14.2; MS: *m/z* 291 (M^{+}-C_3H_7).

Anal. Calcd for $C_{17}H_{22}N_2O_5$: C, 61.07; H, 6.63; N, 8.38; Found: C, 61.12; H, 6.53; N, 8.45.

Ethyl (±)-1-Cyclopropyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (59).

Racemic ester **59** (303 mg, 95%) was prepared as above from **29** (255 mg, 1.00 mmol), cyclopropylamine (57 mg, 1.00 mmol) and acetaldehyde (53 mg, 1.20 mmol) isolated as a yellow solid; mp 161-162 ^{o}C: IR: 1656, 1635, 1495, 1318 cm^{-1}; ^{1}H NMR: δ 12.10 (s, 1H), 8.49 (d, *J* = 2.8Hz, 1H), 8.13 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.04 (d, *J* = 9.2 Hz, 1H), 4.57 (q, *J* = 6.0 Hz, 1H), 4.32 (m, 2H), 2.65 (m, 1H), 1.37 (t, *J* = 7.1), 1.24 (d, *J* = 6.0 Hz, 3H), 1.10 (m, 1H), 0.99 (m, 1H), 0.80 (m, 1H), 0.65 (m, 1H); ^{13}C NMR: δ 169.6, 160.7, 151.9,

138.4, 127,8, 121.4, 116.2, 113.1, 98.9, 60.9, 53.0, 29.4, 18.8, 14.3, 10.4, 7.6; MS: *m/z* 318 (M^+).

Anal. Calcd for $C_{16}H_{18}N_2O_5$: C, 60.37; H, 5.70; N, 8.80; Found: C, 60.47; H, 5.53; N, 8.65.

Ethyl (±)-1-Allyl-2-methyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (60).

Racemic ester **60** (300 mg, 94%) was prepared as above from **29** (255 mg, 1.00 mmol), allylamine (57 mg, 1.00 mmol) and acetaldehyde (53 mg, 1.00 mmol) isolated as a yellow solid; mp 128-130 ^oC: IR: 1662, 1629, 1567, 1492, 1337 cm^{-1}; ^1H NMR: δ 12.16 (s, 1H), 8.51 (d, *J* = 2.8 Hz, 1H), 8.06 (dd, *J* = 9.2, 2.8 Hz, 1H), 6.52 (d, *J* = 9.2 Hz, 1H), 5.85 (ddt, *J* = 17.4, 10.1, 5.0 Hz, 1H), 5.30 (d, *J* = 17.4 Hz, 1H), 5.29 (d, *J* = 10.1 Hz, 1H), 4.56 (q, *J* = 6.0 Hz, 1H), 4.31 (m, 2H), 4.11 (dd, *J* = 16.9, 5.0 Hz, 1H), 3.99 (dd, *J* = 16.9, 5.0 Hz, 1H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.25 (d, *J* = 6.0 Hz, 3H) ; ^{13}C NMR: δ 169.8, 160.9, 150.2, 137.4, 132.1, 128.2, 121.9, 117.9, 115.0, 111.5, 97.7, 54.3, 52.4, 21.1, 14.2; MS: *m/z* 318 (M^+).

Anal. Calcd for $C_{16}H_{18}N_2O_5$: C, 60.37; H, 5.70; N, 8.80; Found: C, 60.47; H, 5.53; N, 8.65.

1-Phenyl-*N*-(propan-2-ylidene)methanamine (63)

To a 250-mL round-bottomed flask equipped with a Dean-Stark trap was added benzylamine (**31**) (0.50 g, 4.66 mmol) and acetone (0.35 g, 6.00 mmol) in 100 mL of benzene. The reaction was refluxed for 24 h, and solvent was removed to afford an oil. Vacuum distillation gave **63** as a colorless oil bp 64-67 ^{o}C, 1.2 mm, IR: 1666, 1493, 1373 cm^{-1}; ^{1}H NMR: δ 7.30 (m, 5H), 4.44 (s, 2H), 2.08 (s, 3H), 1.92 (s, 3H); ^{13}C NMR: δ 168.1, 140.2, 128.3, 127.7, 126.9, 126.4, 55.3, 29.3, 18.7.

***tert*-Butyl 1-Benzyl-6-nitro-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (64).**

In a 100-mL round-bottomed flask was dissolved 300 mg (0.65 mmol) of **33** in 40 mL of CH_2Cl_2. To this was added 3 g of MnO_2, and the reaction was stirred for 3 days.[44] The reaction was worked up by filtering out the solid through a pad of Celite® followed by column chromatography using 30% ether/hexanes to afford 178 mg of **64**; mp 89-91 ^{o}C: IR:1725, 1630, 1612, 1525, 1343 cm^{-1}; ^{1}H NMR: δ 9.33 (d, *J* = 2.9, 1H), 8.30 (dd, *J* = 9.5, 2.9, 1H), 7.38 (m, 10H), 6.98 (m, 1H), 5.25 (s, 2H), 1.19 (s, 9H); ^{13}C NMR: δ 173.3, 164.0, 152.6, 143.8, 143.6, 134.7, 132.0, 130.3, 129.2, 128.7, 128.5, 128.1, 126.6, 125.3, 123.5, 122.2, 118.8, 82.1, 52.5, 27.5; MS: *m/z*. 365 (M^{+} -C_7H_7).

Anal. Calcd for $C_{27}H_{24}N_2O_5$: C, 71.04; H, 5.30; N, 6.14; Found: C, 70.58; H, 5.43; N, 6.05.

***tert*-Butyl (±)-1-Benzyl-3-methyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (65).**

In a 250-mL round-bottomed flask, *tert*-butyl (±)-1-benzyl-2-phenyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (**33**) (1.00 g, 5.50 mmol) was stirred with 2.00 g of anhydrous K_2CO_3 and 0.6 mL of CH_3I in 100 mL of acetone for 1.5 h. The reaction was filtered through a pad of Celite® to remove the solid K_2CO_3. Water (200 mL) was added to the filtrate, and the mixture was extracted twice with 100 mL of CH_2Cl_2. The combined organic layers were washed with saturated NaCl (1x), dried ($MgSO_4$) and concentrated to yield **65** (2.15 g, 99%) as a yellow solid; mp 142-144 ^oC: IR: 1723, 1686, 1605, 1508, 1315 cm^{-1}; ^1H NMR: δ 8.91 (d, *J* = 3.0 Hz, 1H), 8.18 (dd, *J* = 9.4, 3.0 Hz, 1H), 7.26 (m, 10H), 6.82 (d, *J* = 9.4 Hz, 1H), 4.72 (d, *J* = 16.2 Hz, 1H), 4.51 (s, 1H), 4.25 (d, *J* = 16.2 Hz, 1H), 1.58(s, 3H), 1.09 (s, 9H); ^{13}C NMR: δ 189.7, 168.1, 153.0, 138.5, 135.3, 130.3, 129.0, 128.8, 128.1, 126.9, 125.5, 116.9, 113.4, 82.2, 71.9, 58.5, 53.5, 27.2, 22.8; MS: *m/z* 381 (M^+-C_7H_7).

Anal. Calcd for $C_{28}H_{28}N_2O_5$: C, 71.17; H, 5.97; N, 5.93; Found: C, 71.58; H, 5.73; N, 6.05.

(±)-1-Benzyl-3-methyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (66).

tert-Butyl (±)-1-benzyl-3-methyl-2-phenyl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinoline-3-carboxylate (**65**) (0.210 g, 0.44 mmol) was stirred with approximately 1 mL of CF_3CO_2H in CH_2Cl_2 for 1.5 h in a 100-mL, round-bottomed flask. The reaction was added to water

and extracted with CH_2Cl_2 and the organic layer was washed with saturated NaCl (1x), dried ($MgSO_4$) and concentrated to yield the desired product as a yellow solid, which was used without purification in the next reaction; mp 78 ^oC dec: IR: 3500-2417, 1758, 1606, 1510, 1317 cm^{-1}; ^1H NMR: δ 12.31 (bs 1H), 8.87 (d, *J* = 2.6 Hz, 1H), 8.28 (dd, *J* = 9.4, 2.6 Hz, 1H), 7.27 (m 10H), 6.94 (d, *J* = 9.4 Hz, 1H), 4.96 (s, 1H), 4.84 (d, *J* = 16.4 Hz, 1H), 4.31 (d, *J* = 16.4 Hz, 1H), 1.75 (s, 3H); ^{13}C NMR: δ 197.7, 170.5, 153.4, 138.5, 134.9, 134.7, 132.2, 129.6, 129.3, 128.6, 127.6, 126.9, 125.9, 114.7, 113.1, 69.3, 53.9, 53.8, 25.3;

(±)-1-Benzyl-3-methyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline (67).

The carboxylic acid (**66**) from the previous reaction was heated as a solid in a 100 mL round-bottomed flask with an oil bath at 80 ^oC for 45 min until gas evolution ceased to yield **67** (165mg, 100% over two steps); mp 158-161 ^oC: IR: 1690, 1605, 1509, 1320 cm^{-1}; ^1H NMR: δ 8.74 (d, *J* = 3.0 Hz, 1H), 8.13 (dd, *J* = 9.4, 3.0 Hz, 1H), 7.31 (m, 8H), 7.07 (d, *J* = 7.3 Hz, 2H), 6.67 (d, *J* = 9.4 Hz, 1H), 4.75 (d, *J* = 17.1 Hz, 1H), 4.69 (d, *J* = 6.8 Hz, 1H), 4.36 (d, *J* = 17.1 Hz, 1H), 3.52 (quintet, *J* = 6.8 Hz, 1H), 1.05 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR: δ 193.1, 153.8, 137.7, 135.7, 130.3, 129.2, 129.0, 128.9, 128.0, 127.4, 126.2, 126.0, 124.2, 118.1, 112.2, 68.5, 53.6, 45.2, 10.8; MS: *m/z.* 281 (M^+-C_7H_7).

Anal. Calcd for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52; Found: C, 74.58; H, 5.33; N, 7.35.

Structure Elucidation of (±)-1-Benzyl-3-methyl-6-nitro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline (67).

Crystals of **67** were obtained as yellow square rods by vapor diffusion of diethyl ether into a solution of **67** in methylene chloride. A specimen measuring 0.72 x 0.13 x 0.11 mm was mounted on a nylon loop. X-ray intensity data were measured at 296 K on a Bruker SMART APEX II diffractometer. Graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å, fine-focus sealed tube) was used with the CCD detector placed at 6.0 cm. Data frames were collected in a series of ϕ and ω scans with 0.5^{o} and 90-second exposure times. Data integration employed the Bruker SAINT software package.[47] Data were corrected for absorption effects using SADABS multi-scan technique. The structure was solved by direct methods and refined by full-matrix least squares on F^2 using the Buker SHELXTL software suite. The H atoms were placed in calculated positions and allowed to ride on their carrier atoms with C—H = 0.93–0.96 Å and with $U_{iso} = 1.2U_{eq}$(C) for CH and CH_2. Refined Formula: $C_{23}H_{20}N_2O_3$, M_r = 372.41, Monoclinic, space group $P2_1/c$, a = 10.2866 (15) Å, b = 14.519 (2) Å, c = 13.425 (2) Å, α = 90°, β = 107.804 (5)°, γ = 90°, V = 1909.0 (5) $Å^3$, Z = 2, D_x = 1.296 Mg m^{-3}, μ = 0.09 mm^{-1}, T = 296 K, 4741 independent reflections (R_{int} = 0.040), 3123 reflections with $I > 2\sigma(I)$, Final $R[F^2 > 2\sigma(F^2)]$ = 0.044, $wR(F^2)$ = 0.125.

1-Benzyl-3-methyl-6-nitro-2-phenylquinolin-4(1*H*)-one (68).

In a 100-mL round-bottomed flask was dissolved **67** (100 mg, 0.26 mmol) in 40 mL of CH_2Cl_2. To this was added 1.00 g of MnO_2 and the reaction was stirred for 3 days. The

MnO_2 was removed by filtering the reaction through a pad of Celite® followed by column chromatography on silica gel using 30% ether in hexanes to afford 51 mg of **68**; mp 160-162 ^oC. IR: 1735, 1626, 1608, 1520, 1339 cm^{-1}; ^1H NMR: δ 9.36 (d, *J* = 2.74 Hz, 1H), 8.26 (dd, *J* = 9.34, 2.74 Hz, 1H), 7.37 (m, 10H), 6.91 (d, *J* = 9.34 Hz, 1H), 5.22 (s 2H), 1.87 (s, 3H); ^{13}C NMR: δ 177.0, 152.3, 143.6, 143.0, 135.3, 134.1, 129.7, 129.3, 129.1, 127.9, 127.8, 125.9, 125.2, 124.6, 123.8, 120.7, 118.2, 52.8, 30.3; MS: *m/z*. 279 (M^+-C_7H_7).

Anal. Calcd for $C_{27}H_{24}N_2O_5$: C, 71.04; H, 5.30; N, 6.14; Found: C, 70.58; H, 5.43; N, 6.05.

Structure Elucidation of 1-Benzyl-3-methyl-6-nitro-2-phenylquinolin-4(1*H*)-one (68).

Crystals of **68** were obtained as yellow square rods by vapor diffusion of diethyl ether into a solution of **68** in methylene chloride. A specimen measuring 0.28 x 0.15 x 0.10 mm was mounted on a nylon loop. X-ray intensity data were measured at 296 K on a Bruker SMART APEX II diffractometer. Graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å, fine-focus sealed tube) was used with the CCD detector placed at 6.0 cm. Data frames were collected in a series of ϕ and ω scans with 0.5^o scan widths and 30-second exposure times. Data integration employed the Bruker SAINT software package.[47] Data were corrected for absorption effects using SADABS multi-scan technique. The structure was solved by direct methods and refined by full-matrix least squares on F^2 using the Buker SHELXTL software suite. The H atoms were placed in

calculated positions and allowed to ride on their carrier atoms with C—H = 0.93–0.96 Å and with U_{iso} = 1.2U_{eq}(C) for CH and CH_2. Refined Formula: $C_{23}H_{18}N_2O_3$, M_r = 370.39, Monoclinic, space group $P2_1/c$, a = 7.3207 (12) Å, b = 18.984 (3) Å, c = 26.804 (4) Å, α = 90°, β = 96.715 (4)°, γ = 90°, V = 3699.6 (10) $Å^3$, Z = 8, D_x = 1.330 Mg m^{-3}, μ = 0.09 mm^{-1}, T = 296 K, 7575 independent reflections (R_{int} = 0.081), 3498 reflections with $I > 2\sigma(I)$, Final $R[F^2 > 2\sigma(F^2)]$ = 0.048, $wR(F^2)$ = 0.132.

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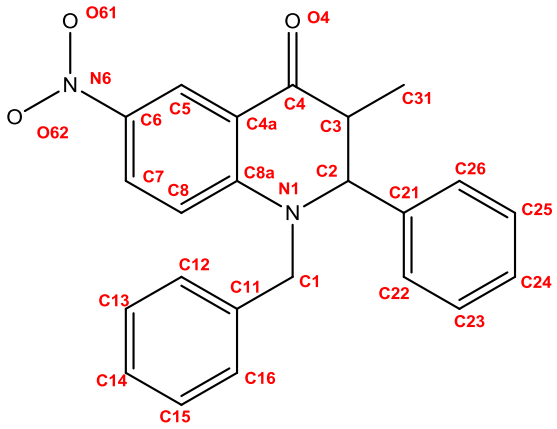
APPPENDICES

CRYSTAL DATA AND STRUCTURE REFINEMENT FOR (±)-1-BENZYL-3-METHYL-6-NITRO-4-OXO-2-PHENYL-1,2,3,4-TETRAHYDROQUINOLINE (67)



Labelling scheme used for refinement of the compound

Crystal data

$C_{23}H_{20}N_2O_3$	$F(000)$ = 784
M_r = 372.41	101(2)
Monoclinic, $P2_1/c$	D_x = 1.296 Mg m^{-3}
Hall symbol: -P 2ybc	Mo $K\alpha$ radiation, λ = 0.71073 Å
a = 10.2866 (15) Å	Cell parameters from 4741 reflections
b = 14.519 (2) Å	θ = 2.1–28.3°
c = 13.425 (2) Å	μ = 0.09 mm^{-1}
β = 107.804 (5)°	T = 296 K
V = 1909.0 (5) Å^3	Square rod, yellow
Z = 4	0.72 × 0.13 × 0.11 mm

Data collection

Bruker SMART APEX II diffractometer	4741 independent reflections
Radiation source: fine-focus sealed tube	3123 reflections with $I > 2\sigma(I)$
graphite	$R_{int} = 0.040$
Detector resolution: 83.33 pixels mm^{-1}	$\theta_{max} = 28.3°$, $\theta_{min} = 2.1°$
ϕ and ω scans with κ offsets	$h = -13 \rightarrow 13$
Absorption correction: multi-scan (*SADABS*; Bruker, 2001)	$k = -19 \rightarrow 18$
$T_{min} = 0.940$, $T_{max} = 0.990$	$l = -17 \rightarrow 17$
29379 measured reflections	

Refinement

Refinement on F^2	Primary atom site location: structure-invariant direct methods
Least-squares matrix: full	Secondary atom site location: difference Fourier map
$R[F^2 > 2\sigma(F^2)] = 0.044$	Hydrogen site location: inferred from neighbouring sites
$wR(F^2) = 0.125$	H-atom parameters not refined
$S = 1.02$	$w = 1/[\sigma^2(F_o^2) + (0.0507P)^2 + 0.3644P]$ where $P = (F_o^2 + 2F_c^2)/3$
4741 reflections	$(\Delta/\sigma)_{max} < 0.001$
253 parameters	$\Delta\rangle_{max} = 0.18$ e $Å^{-3}$
0 restraints	$\Delta\rangle_{min} = -0.15$ e $Å^{-3}$

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

FRACTIONAL ATOMIC COORDINATES AND ISOTROPIC OR EQUIVALENT ISOTROPIC DISPLACEMENT PARAMETERS FOR (±)-1-BENZYL-3-METHYL-6-NITRO-4-OXO-2-PHENYL-1,2,3,4-TETRAHYDROQUINOLINE (67)

	x	*y*	*z*	U_{iso}*/U_{eq}
N1	0.84872 (11)	0.08608 (7)	0.69911 (9)	0.0444 (3)
C2	0.77001 (13)	0.00045 (9)	0.69363 (11)	0.0431 (3)
H2	0.6734	0.0180	0.6729	0.052*
C3	0.78890 (14)	-0.06152 (9)	0.60661 (11)	0.0449 (3)
H3	0.7573	-0.0255	0.5419	0.054*
C4	0.93834 (14)	-0.07929 (9)	0.62432 (11)	0.0462 (3)
C4A	1.02434 (13)	0.00376 (9)	0.65157 (10)	0.0423 (3)
C5	1.15598 (14)	0.00170 (10)	0.64500 (10)	0.0477 (3)
H5	1.1901	-0.0522	0.6251	0.057*
C6	1.23628 (14)	0.07907 (11)	0.66780 (11)	0.0514 (4)
C7	1.18453 (16)	0.16163 (11)	0.69206 (12)	0.0567 (4)
H7	1.2385	0.2143	0.7040	0.068*
C8	1.05469 (15)	0.16563 (10)	0.69842 (12)	0.0521 (4)
H8	1.0202	0.2214	0.7132	0.063*
C8A	0.97219 (13)	0.08583 (9)	0.68283 (10)	0.0417 (3)
C1	0.79149 (15)	0.16967 (9)	0.72869 (11)	0.0481 (3)
H1A	0.8622	0.2010	0.7828	0.058*
H1B	0.7197	0.1528	0.7582	0.058*
C11	0.73349 (13)	0.23568 (9)	0.63886 (12)	0.0475 (3)
C12	0.7230 (2)	0.32758 (12)	0.65934 (16)	0.0787 (5)
H12	0.7529	0.3483	0.7281	0.094*
C13	0.6687 (3)	0.38972 (14)	0.5794 (2)	0.1017 (8)
H13	0.6631	0.4518	0.5949	0.122*
C14	0.6232 (2)	0.36066 (15)	0.4780 (2)	0.0867 (6)
H14	0.5861	0.4025	0.4244	0.104*
C15	0.6325 (2)	0.27003 (15)	0.45599 (16)	0.0789 (5)
H15	0.6017	0.2497	0.3870	0.095*
C16	0.68789 (18)	0.20786 (12)	0.53593 (13)	0.0656 (4)
H16	0.6944	0.1461	0.5198	0.079*
C21	0.80118 (14)	-0.04741 (9)	0.79944 (11)	0.0458 (3)
C22	0.93358 (17)	-0.06631 (11)	0.86172 (12)	0.0587 (4)
H22	1.0069	-0.0470	0.8402	0.070*

C23	0.9579 (2)	-0.11326 (13)	0.95485 (13)	0.0697 (5)
H23	1.0471	-0.1262	0.9949	0.084*
C24	0.8517 (2)	-0.14083 (12)	0.98858 (14)	0.0720 (5)
H24	0.8685	-0.1718	1.0519	0.086*
C25	0.7202 (2)	-0.12274 (12)	0.92876 (16)	0.0752 (5)
H25	0.6477	-0.1415	0.9516	0.090*
C26	0.69477 (17)	-0.07656 (11)	0.83438 (13)	0.0611 (4)
H26	0.6052	-0.0651	0.7941	0.073*
C31	0.70126 (17)	-0.14768 (11)	0.58841 (14)	0.0623 (4)
H31A	0.6076	-0.1308	0.5772	0.093*
H31B	0.7313	-0.1871	0.6485	0.093*
H31C	0.7094	-0.1796	0.5280	0.093*
O4	0.98439 (12)	-0.15461 (7)	0.61428 (10)	0.0672 (3)
N6	1.37607 (14)	0.07422 (13)	0.66627 (11)	0.0677 (4)
O61	1.45000 (13)	0.14153 (12)	0.69692 (12)	0.0978 (5)
O62	1.41522 (12)	0.00257 (11)	0.63471 (11)	0.0861 (4)

ATOMIC DISPLACEMENT PARAMETERS FOR (±)-1-BENZYL-3-METHYL-6-NITRO-4-OXO-2-PHENYL-1,2,3,4-TETRAHYDROQUINOLINE (67)

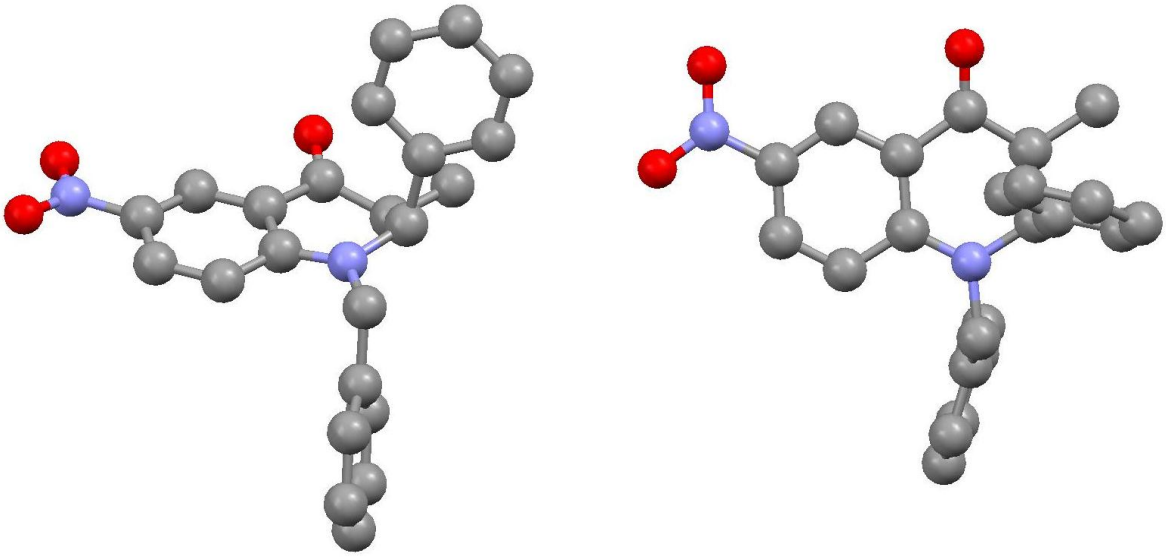
	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0452 (6)	0.0387 (6)	0.0542 (7)	0.0013 (5)	0.0225 (5)	0.0022 (5)
C2	0.0384 (6)	0.0421 (7)	0.0506 (8)	0.0004 (5)	0.0164 (6)	0.0049 (6)
C3	0.0463 (7)	0.0447 (7)	0.0429 (7)	-0.0032 (6)	0.0123 (6)	0.0020 (6)
C4	0.0521 (8)	0.0441 (8)	0.0444 (7)	0.0017 (6)	0.0176 (6)	-0.0010 (6)
C4A	0.0420 (7)	0.0448 (7)	0.0414 (7)	0.0020 (6)	0.0148 (5)	0.0035 (6)
C5	0.0450 (7)	0.0578 (9)	0.0425 (7)	0.0077 (6)	0.0167 (6)	0.0066 (6)
C6	0.0381 (7)	0.0720 (10)	0.0454 (8)	-0.0019 (7)	0.0145 (6)	0.0066 (7)
C7	0.0542 (9)	0.0608 (10)	0.0562 (9)	-0.0175 (7)	0.0187 (7)	-0.0009 (7)
C8	0.0549 (8)	0.0457 (8)	0.0596 (9)	-0.0052 (6)	0.0232 (7)	-0.0007 (7)
C8A	0.0423 (7)	0.0427 (7)	0.0416 (7)	0.0002 (5)	0.0151 (6)	0.0043 (6)
C1	0.0512 (8)	0.0448 (8)	0.0530 (8)	0.0031 (6)	0.0229 (7)	-0.0025 (6)
C11	0.0395 (7)	0.0428 (8)	0.0625 (9)	0.0002 (6)	0.0192 (6)	0.0008 (6)
C12	0.0907 (14)	0.0508 (10)	0.0832 (13)	0.0117 (9)	0.0098 (10)	-0.0067 (9)
C13	0.1131 (18)	0.0507 (11)	0.126 (2)	0.0198 (11)	0.0138 (15)	0.0090 (12)
C14	0.0724 (12)	0.0755 (14)	0.1042 (17)	0.0083 (10)	0.0151 (11)	0.0367 (12)
C15	0.0814 (13)	0.0852 (14)	0.0658 (12)	-0.0005 (10)	0.0160 (10)	0.0181 (10)
C16	0.0788 (11)	0.0536 (10)	0.0631 (11)	0.0014 (8)	0.0199 (9)	0.0036 (8)
C21	0.0531 (8)	0.0397 (7)	0.0490 (8)	-0.0002 (6)	0.0221 (6)	0.0003 (6)
C22	0.0570 (9)	0.0686 (10)	0.0491 (9)	-0.0045 (7)	0.0143 (7)	0.0075 (7)
C23	0.0768 (11)	0.0736 (11)	0.0516 (9)	-0.0004 (9)	0.0092 (8)	0.0086 (8)
C24	0.1037 (15)	0.0624 (11)	0.0542 (10)	0.0036 (10)	0.0307 (10)	0.0135 (8)
C25	0.0905 (14)	0.0707 (12)	0.0824 (13)	0.0058 (10)	0.0533 (11)	0.0212 (10)
C26	0.0609 (9)	0.0598 (10)	0.0726 (11)	0.0080 (7)	0.0350 (8)	0.0146 (8)
C31	0.0623 (10)	0.0563 (9)	0.0661 (10)	-0.0126 (7)	0.0164 (8)	-0.0037 (8)
O4	0.0652 (7)	0.0491 (6)	0.0876 (8)	0.0053 (5)	0.0239 (6)	-0.0123 (6)
N6	0.0420 (7)	0.1069 (13)	0.0528 (8)	-0.0037 (8)	0.0125 (6)	0.0088 (8)
O61	0.0524 (7)	0.1372 (13)	0.1030 (11)	-0.0311 (8)	0.0226 (7)	-0.0107 (9)
O62	0.0474 (7)	0.1236 (12)	0.0894 (9)	0.0180 (7)	0.0242 (6)	0.0009 (9)

GEOMETRIC PARAMETERS FOR (±)-1-BENZYL-3-METHYL-6-NITRO-4-OXO-2-PHENYL-1,2,3,4-TETRAHYDROQUINOLINE (67)

N1—C8A	1.3530 (16)	C1—C11	1.513 (2)
N1—C1	1.4561 (17)	C11—C12	1.373 (2)
N1—C2	1.4732 (17)	C11—C16	1.377 (2)
C2—C21	1.5248 (19)	C12—C13	1.382 (3)
C2—C3	1.5333 (19)	C13—C14	1.364 (3)
C3—C4	1.504 (2)	C14—C15	1.359 (3)
C3—C31	1.517 (2)	C15—C16	1.385 (2)
C4—O4	1.2155 (16)	C21—C26	1.382 (2)
C4—C4A	1.4739 (19)	C21—C22	1.390 (2)
C4A—C5	1.3840 (18)	C22—C23	1.378 (2)
C4A—C8A	1.4217 (18)	C23—C24	1.364 (3)
C5—C6	1.372 (2)	C24—C25	1.371 (3)
C6—C7	1.390 (2)	C25—C26	1.386 (2)
C6—N6	1.4460 (19)	N6—O61	1.229 (2)
C7—C8	1.365 (2)	N6—O62	1.236 (2)
C8—C8A	1.4135 (19)		
C8A—N1—C1	121.61 (11)	N1—C8A—C4A	120.50 (12)
C8A—N1—C2	121.22 (11)	C8—C8A—C4A	117.85 (12)
C1—N1—C2	117.08 (10)	N1—C1—C11	113.85 (11)
N1—C2—C21	112.47 (11)	C12—C11—C16	117.54 (15)
N1—C2—C3	109.73 (10)	C12—C11—C1	119.47 (15)
C21—C2—C3	113.76 (11)	C16—C11—C1	122.99 (13)
C4—C3—C31	114.34 (12)	C11—C12—C13	121.1 (2)
C4—C3—C2	109.98 (11)	C14—C13—C12	120.43 (19)
C31—C3—C2	113.51 (12)	C15—C14—C13	119.43 (19)
O4—C4—C4A	122.61 (13)	C14—C15—C16	120.2 (2)
O4—C4—C3	123.43 (13)	C11—C16—C15	121.32 (17)
C4A—C4—C3	113.93 (11)	C26—C21—C22	117.85 (14)
C5—C4A—C8A	120.11 (12)	C26—C21—C2	119.52 (13)
C5—C4A—C4	119.42 (12)	C22—C21—C2	122.58 (12)
C8A—C4A—C4	120.46 (12)	C23—C22—C21	121.05 (15)
C6—C5—C4A	120.15 (13)	C24—C23—C22	120.32 (17)
C5—C6—C7	120.70 (13)	C23—C24—C25	119.73 (16)
C5—C6—N6	119.37 (15)	C24—C25—C26	120.33 (16)

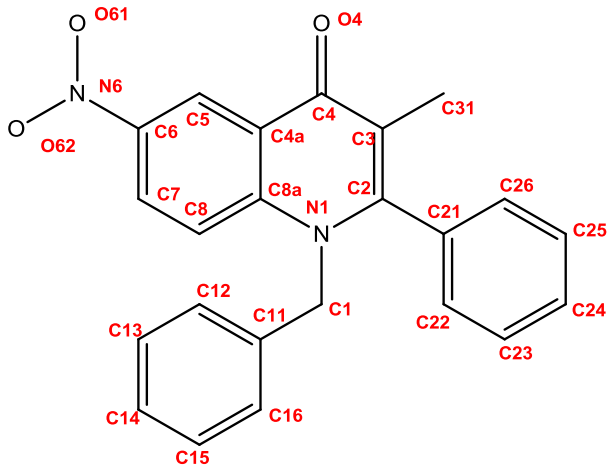
C7—C6—N6	119.93 (14)	C21—C26—C25	120.70 (16)
C8—C7—C6	120.22 (14)	O61—N6—O62	123.41 (15)
C7—C8—C8A	120.69 (14)	O61—N6—C6	118.20 (16)
N1—C8A—C8	121.64 (12)	O62—N6—C6	118.38 (15)
C8A—N1—C2—C21	90.78 (14)	C5—C4A—C8A—C8	4.90 (19)
C1—N1—C2—C21	-85.76 (14)	C4—C4A—C8A—C8	-174.14 (12)
C8A—N1—C2—C3	-36.92 (16)	C8A—N1—C1—C11	76.78 (16)
C1—N1—C2—C3	146.54 (12)	C2—N1—C1—C11	-106.70 (13)
N1—C2—C3—C4	55.74 (14)	N1—C1—C11—C12	-156.22 (15)
C21—C2—C3—C4	-71.24 (14)	N1—C1—C11—C16	24.84 (19)
N1—C2—C3—C31	-174.73 (12)	C16—C11—C12—C13	0.0 (3)
C21—C2—C3—C31	58.30 (16)	C1—C11—C12—C13	-179.04 (18)
C31—C3—C4—O4	7.4 (2)	C11—C12—C13—C14	0.5 (4)
C2—C3—C4—O4	136.46 (14)	C12—C13—C14—C15	-0.4 (4)
C31—C3—C4—C4A	-174.63 (12)	C13—C14—C15—C16	-0.1 (3)
C2—C3—C4—C4A	-45.54 (15)	C12—C11—C16—C15	-0.5 (2)
O4—C4—C4A—C5	13.6 (2)	C1—C11—C16—C15	178.49 (15)
C3—C4—C4A—C5	-164.42 (12)	C14—C15—C16—C11	0.5 (3)
O4—C4—C4A—C8A	-167.37 (13)	N1—C2—C21—C26	131.53 (14)
C3—C4—C4A—C8A	14.62 (18)	C3—C2—C21—C26	-102.93 (15)
C8A—C4A—C5—C6	-0.5 (2)	N1—C2—C21—C22	-50.84 (18)
C4—C4A—C5—C6	178.51 (12)	C3—C2—C21—C22	74.69 (17)
C4A—C5—C6—C7	-3.6 (2)	C26—C21—C22—C23	0.5 (2)
C4A—C5—C6—N6	176.52 (12)	C2—C21—C22—C23	-177.13 (15)
C5—C6—C7—C8	3.1 (2)	C21—C22—C23—C24	-1.1 (3)
N6—C6—C7—C8	-176.94 (13)	C22—C23—C24—C25	0.9 (3)
C6—C7—C8—C8A	1.4 (2)	C23—C24—C25—C26	-0.1 (3)
C1—N1—C8A—C8	3.0 (2)	C22—C21—C26—C25	0.3 (2)
C2—N1—C8A—C8	-173.38 (12)	C2—C21—C26—C25	178.01 (15)

C1—N1—C8A—C4A	-178.49 (12)	C24—C25—C26—C21	-0.5 (3)
C2—N1—C8A—C4A	5.13 (19)	C5—C6—N6—O61	-172.90 (14)
C7—C8—C8A—N1	173.21 (13)	C7—C6—N6—O61	7.2 (2)
C7—C8—C8A—C4A	-5.3 (2)	C5—C6—N6—O62	6.8 (2)
C5—C4A—C8A—N1	-173.67 (12)	C7—C6—N6—O62	-173.13 (14)
C4—C4A—C8A—N1	7.29 (19)		



Two views of (**67**)

CRYSTAL DATA AND STRUCTURE REFINEMENT FOR 1-BENZYL-3-METHYL-6-NITRO-2-PHENYLQUINOLIN-4(1*H*)-ONE (68)



Labelling scheme used for refinement of the compound

Crystal data

$C_{23}H_{18}N_2O_3$	$F(000)$ = 1552
M_r = 370.39	D_x = 1.330 Mg m^{-3}
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation, λ = 0.71073 Å
Hall symbol: -P 2ybc	Cell parameters from 7575 reflections
a = 7.3207 (12) Å	θ = 1.9–26.4°
b = 18.984 (3) Å	μ = 0.09 mm^{-1}
c = 26.804 (4) Å	T = 296 K
β = 96.715 (4)°	Shard, yellow
V = 3699.6 (10) Å^3	0.28 × 0.15 × 0.10 mm
Z = 8	

Data collection

Bruker SMART APEX II diffractometer	7575 independent reflections
Radiation source: fine-focus sealed tube	3498 reflections with $I > 2\sigma(I)$
graphite	$R_{int} = 0.081$
Detector resolution: 83.33 pixels mm^{-1}	$\theta_{max} = 26.4°$, $\theta_{min} = 1.9°$
ϕ and ω scans with κ offsets	$h = -9 \rightarrow 9$
Absorption correction: multi-scan *SADABS* (Bruker, 2001)	$k = -23 \rightarrow 16$
$T_{min} = 0.976$, $T_{max} = 0.991$	$l = -33 \rightarrow 31$
45838 measured reflections	

Refinement

Refinement on F^2	Primary atom site location: structure-invariant direct methods
Least-squares matrix: full	Secondary atom site location: difference Fourier map
$R[F^2 > 2\sigma(F^2)] = 0.048$	Hydrogen site location: inferred from neighbouring sites
$wR(F^2) = 0.132$	H-atom parameters not refined
$S = 0.98$	$w = 1/[\sigma^2(F_o^2) + (0.0519P)^2 + 0.1781P]$ where $P = (F_o^2 + 2F_c^2)/3$
7575 reflections	$(\Delta/\sigma)_{max} < 0.001$
505 parameters	$\Delta\rangle_{max} = 0.14$ e $Å^{-3}$
0 restraints	$\Delta\rangle_{min} = -0.17$ e $Å^{-3}$

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R- factors based on ALL data will be even larger.

FRACTIONAL ATOMIC COORDINATES AND ISOTROPIC OR EQUIVALENT ISOTROPIC DISPLACEMENT PARAMETERS FOR 1-BENZYL-3-METHYL-6-NITRO-2-PHENYLQUINOLIN-4(1*H*)-ONE (68)

	x	*y*	*z*	U_{iso}*/U_{eq}	Occ. (<1)
N1A	-0.0529 (2)	0.23303 (10)	-0.00425 (7)	0.0497 (5)	
C2A	-0.0326 (3)	0.30546 (12)	0.00048 (9)	0.0497 (6)	
C3A	-0.0083 (3)	0.33853 (12)	0.04562 (9)	0.0499 (6)	
C4A	-0.0053 (3)	0.29893 (12)	0.09134 (9)	0.0512 (6)	
C4AA	-0.0451 (3)	0.22362 (12)	0.08545 (8)	0.0454 (5)	
C5A	-0.0597 (3)	0.18285 (13)	0.12764 (9)	0.0542 (6)	
H5A	-0.0429	0.2032	0.1594	0.065*	
C6A	-0.0991 (3)	0.11252 (14)	0.12243 (9)	0.0561 (6)	
C7A	-0.1243 (3)	0.08039 (13)	0.07559 (10)	0.0618 (7)	
H7A	-0.1515	0.0326	0.0728	0.074*	
C8A	-0.1087 (3)	0.12010 (13)	0.03346 (9)	0.0576 (6)	
H8A	-0.1248	0.0990	0.0019	0.069*	
C8AA	-0.0685 (3)	0.19222 (12)	0.03770 (9)	0.0472 (6)	
C1A	-0.0234 (3)	0.19819 (12)	-0.05200 (8)	0.0564 (6)	
H1A1	0.0568	0.1580	-0.0442	0.068*	
H1A2	0.0414	0.2309	-0.0715	0.068*	
C11A	-0.1930 (3)	0.17284 (11)	-0.08476 (9)	0.0534 (6)	
C12A	-0.1671 (4)	0.13803 (13)	-0.12868 (10)	0.0761 (8)	
H12A	-0.0488	0.1320	-0.1374	0.091*	
C13A	-0.3158 (5)	0.11223 (16)	-0.15957 (11)	0.0938 (10)	
H13A	-0.2973	0.0897	-0.1894	0.113*	
C14A	-0.4896 (5)	0.11940 (16)	-0.14687 (13)	0.0931 (10)	
H14A	-0.5893	0.1008	-0.1674	0.112*	
C15A	-0.5157 (4)	0.15419 (16)	-0.10368 (12)	0.0838 (9)	
H15A	-0.6340	0.1594	-0.0948	0.101*	
C16A	-0.3684 (4)	0.18160 (13)	-0.07309 (9)	0.0675 (7)	
H16A	-0.3885	0.2063	-0.0443	0.081*	
C21A	-0.0470 (3)	0.34714 (11)	-0.04724 (8)	0.0510 (6)	
C22A	-0.2189 (3)	0.36206 (13)	-0.07160 (9)	0.0615 (7)	
H22A	-0.3232	0.3443	-0.0593	0.074*	
C23A	-0.2364 (4)	0.40332 (13)	-0.11421 (10)	0.0692 (7)	
H23A	-0.3526	0.4133	-0.1305	0.083*	

C24A	-0.0833 (4)	0.42964 (13)	-0.13259 (10)	0.0698 (7)	
H24A	-0.0958	0.4571	-0.1615	0.084*	
C25A	0.0879 (4)	0.41550 (13)	-0.10844 (10)	0.0669 (7)	
H25A	0.1916	0.4337	-0.1209	0.080*	
C26A	0.1074 (3)	0.37421 (12)	-0.06561 (9)	0.0599 (6)	
H26A	0.2239	0.3647	-0.0492	0.072*	
C31A	0.0148 (4)	0.41726 (12)	0.05038 (10)	0.0750 (8)	
H31A	0.0307	0.4301	0.0853	0.113*	0.50
H31B	-0.0925	0.4402	0.0339	0.113*	0.50
H31C	0.1210	0.4316	0.0350	0.113*	0.50
H31D	0.0088	0.4379	0.0175	0.113*	0.50
H31E	0.1320	0.4277	0.0689	0.113*	0.50
H31F	-0.0815	0.4363	0.0677	0.113*	0.50
O4A	0.0252 (2)	0.32635 (9)	0.13352 (6)	0.0727 (5)	
N6A	-0.1184 (3)	0.07021 (15)	0.16727 (10)	0.0758 (7)	
O61A	-0.1144 (3)	0.10018 (12)	0.20774 (8)	0.0997 (7)	
O62A	-0.1405 (3)	0.00701 (13)	0.16238 (9)	0.1175 (8)	
N1B	0.5350 (2)	0.27874 (10)	0.16217 (7)	0.0523 (5)	
C2B	0.5447 (3)	0.34572 (12)	0.14161 (9)	0.0509 (6)	
C3B	0.5183 (3)	0.35775 (12)	0.09143 (9)	0.0518 (6)	
C4B	0.4776 (3)	0.30075 (13)	0.05656 (10)	0.0529 (6)	
C4AB	0.4529 (3)	0.23157 (12)	0.07939 (9)	0.0479 (6)	
C5B	0.3994 (3)	0.17425 (13)	0.04839 (9)	0.0554 (6)	
H5B	0.3798	0.1799	0.0137	0.066*	
C6B	0.3759 (3)	0.10982 (13)	0.06940 (10)	0.0578 (6)	
C7B	0.4044 (3)	0.09883 (13)	0.12080 (10)	0.0628 (7)	
H7B	0.3876	0.0544	0.1341	0.075*	
C8B	0.4575 (3)	0.15426 (13)	0.15156 (9)	0.0594 (6)	
H8B	0.4778	0.1474	0.1861	0.071*	
C8AB	0.4820 (3)	0.22208 (12)	0.13141 (9)	0.0497 (6)	
C1B	0.5931 (3)	0.26597 (12)	0.21614 (8)	0.0583 (6)	
H1B1	0.6607	0.3069	0.2299	0.070*	
H1B2	0.6772	0.2263	0.2192	0.070*	
C11B	0.4395 (3)	0.25123 (12)	0.24759 (9)	0.0540 (6)	
C12B	0.2629 (3)	0.27454 (14)	0.23456 (10)	0.0731 (8)	
H12B	0.2328	0.2985	0.2044	0.088*	
C13B	0.1295 (4)	0.26256 (16)	0.26606 (12)	0.0852 (9)	

H13B	0.0108	0.2793	0.2572	0.102*	
C14B	0.1699 (4)	0.22653 (16)	0.30995 (11)	0.0841 (9)	
H14B	0.0791	0.2179	0.3307	0.101*	
C15B	0.3459 (5)	0.20319 (15)	0.32302 (11)	0.0856 (9)	
H15B	0.3751	0.1789	0.3530	0.103*	
C16B	0.4799 (4)	0.21526 (13)	0.29223 (10)	0.0697 (7)	
H16B	0.5989	0.1990	0.3015	0.084*	
C21B	0.5837 (3)	0.40577 (12)	0.17742 (8)	0.0560 (6)	
C22B	0.7615 (4)	0.42954 (13)	0.19050 (9)	0.0667 (7)	
H22B	0.8591	0.4066	0.1782	0.080*	
C23B	0.7949 (4)	0.48672 (15)	0.22147 (10)	0.0778 (8)	
H23B	0.9149	0.5019	0.2306	0.093*	
C24B	0.6515 (6)	0.52146 (15)	0.23901 (11)	0.0882 (10)	
H24B	0.6746	0.5609	0.2593	0.106*	
C25B	0.4752 (5)	0.49882 (17)	0.22703 (11)	0.0895 (9)	
H25B	0.3788	0.5221	0.2397	0.107*	
C26B	0.4403 (4)	0.44084 (15)	0.19586 (10)	0.0759 (8)	
H26B	0.3200	0.4255	0.1873	0.091*	
C31B	0.5289 (4)	0.43038 (13)	0.06906 (10)	0.0768 (8)	
H31G	0.5057	0.4274	0.0331	0.115*	0.50
H31H	0.6492	0.4497	0.0784	0.115*	0.50
H31I	0.4384	0.4603	0.0814	0.115*	0.50
H31J	0.5565	0.4642	0.0955	0.115*	0.50
H31K	0.4130	0.4419	0.0502	0.115*	0.50
H31L	0.6238	0.4313	0.0472	0.115*	0.50
O4B	0.4620 (2)	0.30779 (9)	0.01016 (7)	0.0702 (5)	
N6B	0.3157 (3)	0.05041 (14)	0.03641 (11)	0.0773 (7)	
O61B	0.2910 (3)	0.06085 (11)	-0.00890 (9)	0.0986 (7)	
O62B	0.2858 (4)	-0.00533 (11)	0.05574 (9)	0.1232 (9)	

ATOMIC DISPLACEMENT PARAMETERS FOR 1-BENZYL-3-METHYL-6-NITRO-2-PHENYLQUINOLIN-4(1*H*)-ONE (68)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1A	0.0604 (11)	0.0483 (12)	0.0408 (12)	-0.0036 (9)	0.0073 (8)	-0.0066 (10)
C2A	0.0515 (13)	0.0469 (15)	0.0508 (16)	-0.0024 (11)	0.0066 (11)	-0.0027 (13)
C3A	0.0534 (13)	0.0463 (14)	0.0489 (16)	-0.0010 (10)	0.0010 (11)	-0.0050 (13)
C4A	0.0477 (12)	0.0568 (16)	0.0480 (16)	0.0063 (11)	0.0013 (11)	-0.0064 (14)
C4AA	0.0392 (11)	0.0536 (15)	0.0434 (15)	0.0032 (10)	0.0050 (10)	0.0020 (13)
C5A	0.0470 (13)	0.0658 (17)	0.0496 (16)	0.0019 (11)	0.0042 (11)	-0.0009 (14)
C6A	0.0490 (13)	0.0643 (18)	0.0552 (17)	0.0014 (12)	0.0076 (11)	0.0144 (15)
C7A	0.0626 (15)	0.0542 (16)	0.0682 (19)	-0.0055 (12)	0.0054 (13)	0.0044 (15)
C8A	0.0637 (15)	0.0556 (17)	0.0529 (17)	-0.0061 (12)	0.0044 (12)	-0.0036 (14)
C8AA	0.0458 (12)	0.0500 (15)	0.0457 (15)	-0.0024 (10)	0.0049 (10)	0.0000 (13)
C1A	0.0703 (15)	0.0529 (15)	0.0489 (15)	0.0013 (12)	0.0189 (12)	-0.0045 (12)
C11A	0.0713 (16)	0.0459 (14)	0.0436 (15)	-0.0045 (12)	0.0094 (12)	-0.0004 (12)
C12A	0.103 (2)	0.0690 (19)	0.0585 (19)	-0.0080 (16)	0.0201 (16)	-0.0178 (16)
C13A	0.145 (3)	0.079 (2)	0.055 (2)	-0.017 (2)	0.001 (2)	-0.0203 (16)
C14A	0.115 (3)	0.087 (2)	0.071 (2)	-0.027 (2)	-0.018 (2)	0.0023 (19)
C15A	0.0774 (19)	0.099 (2)	0.073 (2)	-0.0130 (16)	-0.0017 (16)	0.0049 (19)
C16A	0.0735 (17)	0.0718 (18)	0.0565 (17)	-0.0040 (14)	0.0046 (14)	-0.0046 (14)
C21A	0.0608 (14)	0.0466 (14)	0.0455 (15)	-0.0035 (11)	0.0065 (12)	-0.0021 (12)
C22A	0.0633 (16)	0.0616 (17)	0.0592 (17)	-0.0064 (12)	0.0056 (13)	0.0066 (14)
C23A	0.0742 (18)	0.0653 (18)	0.0653 (19)	0.0014 (14)	-0.0033 (14)	0.0087 (15)
C24A	0.097 (2)	0.0578 (17)	0.0542 (17)	0.0006 (15)	0.0073 (16)	0.0075 (14)
C25A	0.0800 (18)	0.0585 (17)	0.0650 (18)	-0.0085 (13)	0.0205 (15)	0.0045 (14)
C26A	0.0625 (15)	0.0581 (16)	0.0598 (17)	-0.0037 (12)	0.0100 (12)	0.0022 (14)
C31A	0.0930 (19)	0.0567 (18)	0.075 (2)	-0.0027 (14)	0.0063 (15)	-0.0120 (14)
O4A	0.0976 (13)	0.0695 (12)	0.0476 (11)	0.0096 (9)	-0.0059 (9)	-0.0119 (9)
N6A	0.0776 (15)	0.082 (2)	0.0666 (19)	-0.0024 (13)	0.0053 (13)	0.0216 (17)
O61A	0.1293 (18)	0.1081 (18)	0.0621 (14)	0.0031 (13)	0.0126 (12)	0.0222 (13)
O62A	0.169 (2)	0.0785 (17)	0.1058 (19)	-0.0197 (15)	0.0191 (15)	0.0277 (14)
N1B	0.0569 (11)	0.0529 (13)	0.0469 (12)	-0.0048 (9)	0.0053 (9)	0.0040 (11)
C2B	0.0510 (13)	0.0509 (15)	0.0513 (16)	-0.0029 (11)	0.0074 (11)	-0.0001 (13)
C3B	0.0536 (13)	0.0514 (15)	0.0514 (16)	-0.0055 (11)	0.0101 (11)	0.0040 (13)
C4B	0.0440 (12)	0.0620 (17)	0.0532 (17)	-0.0028 (11)	0.0085 (11)	0.0031 (14)
C4AB	0.0371 (11)	0.0566 (15)	0.0505 (16)	-0.0019 (10)	0.0066 (10)	-0.0014 (13)

C5B	0.0469 (13)	0.0624 (17)	0.0569 (16)	-0.0017 (11)	0.0065 (11)	-0.0060 (14)
C6B	0.0546 (14)	0.0517 (16)	0.0672 (19)	-0.0029 (12)	0.0074 (12)	-0.0114 (15)
C7B	0.0656 (15)	0.0494 (16)	0.073 (2)	-0.0048 (12)	0.0058 (13)	0.0022 (15)
C8B	0.0632 (15)	0.0571 (17)	0.0573 (16)	-0.0037 (12)	0.0052 (12)	0.0019 (14)
C8AB	0.0449 (12)	0.0496 (15)	0.0544 (16)	-0.0043 (11)	0.0055 (11)	-0.0029 (13)
C1B	0.0606 (14)	0.0580 (16)	0.0540 (16)	-0.0039 (12)	-0.0034 (12)	0.0046 (13)
C11B	0.0605 (15)	0.0522 (15)	0.0476 (15)	-0.0043 (11)	-0.0002 (12)	-0.0003 (12)
C12B	0.0612 (16)	0.097 (2)	0.0586 (18)	-0.0054 (14)	-0.0031 (14)	0.0161 (15)
C13B	0.0619 (17)	0.115 (3)	0.077 (2)	-0.0080 (16)	0.0046 (16)	0.009 (2)
C14B	0.093 (2)	0.094 (2)	0.069 (2)	-0.0171 (18)	0.0251 (17)	0.0026 (18)
C15B	0.104 (2)	0.087 (2)	0.068 (2)	0.0027 (18)	0.0170 (18)	0.0210 (17)
C16B	0.0770 (18)	0.0692 (18)	0.0621 (19)	0.0071 (14)	0.0046 (15)	0.0135 (15)
C21B	0.0721 (16)	0.0496 (15)	0.0475 (16)	-0.0001 (13)	0.0122 (12)	0.0014 (12)
C22B	0.0805 (18)	0.0638 (17)	0.0590 (17)	-0.0192 (14)	0.0211 (14)	-0.0097 (14)
C23B	0.109 (2)	0.071 (2)	0.0552 (19)	-0.0291 (18)	0.0192 (16)	-0.0096 (16)
C24B	0.156 (3)	0.0560 (19)	0.052 (2)	0.003 (2)	0.011 (2)	-0.0032 (15)
C25B	0.123 (3)	0.081 (2)	0.065 (2)	0.041 (2)	0.0133 (19)	-0.0042 (18)
C26B	0.087 (2)	0.0716 (19)	0.069 (2)	0.0185 (15)	0.0079 (15)	-0.0002 (16)
C31B	0.0883 (18)	0.0688 (19)	0.074 (2)	-0.0107 (15)	0.0100 (15)	0.0105 (16)
O4B	0.0863 (12)	0.0767 (13)	0.0485 (11)	-0.0071 (9)	0.0112 (9)	0.0021 (10)
N6B	0.0823 (16)	0.0656 (18)	0.082 (2)	-0.0031 (13)	-0.0002 (14)	-0.0123 (17)
O61B	0.1338 (18)	0.0835 (15)	0.0768 (15)	-0.0167 (12)	0.0049 (13)	-0.0209 (13)
O62B	0.196 (2)	0.0545 (14)	0.1107 (19)	-0.0221 (15)	-0.0177 (16)	-0.0018 (13)

GEOMETRIC PARAMETERS FOR 1-BENZYL-3-METHYL-6-NITRO-2-PHENYLQUINOLIN-4(1*H*)-ONE (68)

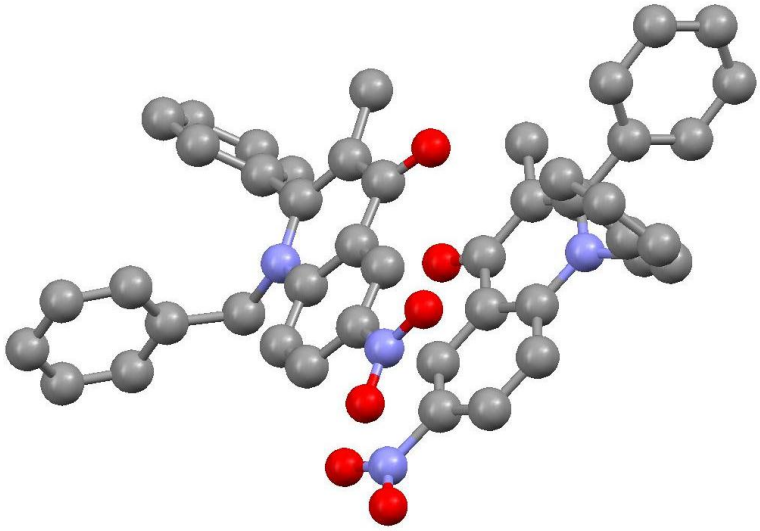
N1A—C8AA	1.381 (3)	N1B—C8AB	1.383 (3)
N1A—C2A	1.387 (3)	N1B—C2B	1.391 (3)
N1A—C1A	1.479 (3)	N1B—C1B	1.479 (3)
C2A—C3A	1.356 (3)	C2B—C3B	1.356 (3)
C2A—C21A	1.497 (3)	C2B—C21B	1.496 (3)
C3A—C4A	1.436 (3)	C3B—C4B	1.438 (3)
C3A—C31A	1.508 (3)	C3B—C31B	1.509 (3)
C4A—O4A	1.241 (2)	C4B—O4B	1.243 (3)
C4A—C4AA	1.464 (3)	C4B—C4AB	1.469 (3)
C4AA—C5A	1.385 (3)	C4AB—C5B	1.397 (3)
C4AA—C8AA	1.404 (3)	C4AB—C8AB	1.397 (3)
C5A—C6A	1.369 (3)	C5B—C6B	1.366 (3)
C6A—C7A	1.389 (3)	C6B—C7B	1.385 (3)
C6A—N6A	1.466 (3)	C6B—N6B	1.469 (3)
C7A—C8A	1.374 (3)	C7B—C8B	1.365 (3)
C8A—C8AA	1.402 (3)	C8B—C8AB	1.416 (3)
C1A—C11A	1.513 (3)	C1B—C11B	1.509 (3)
C11A—C16A	1.367 (3)	C11B—C12B	1.373 (3)
C11A—C12A	1.382 (3)	C11B—C16B	1.379 (3)
C12A—C13A	1.379 (4)	C12B—C13B	1.382 (3)
C13A—C14A	1.361 (4)	C13B—C14B	1.363 (4)
C14A—C15A	1.366 (4)	C14B—C15B	1.369 (4)
C15A—C16A	1.378 (3)	C15B—C16B	1.373 (3)
C21A—C22A	1.378 (3)	C21B—C26B	1.383 (3)
C21A—C26A	1.384 (3)	C21B—C22B	1.383 (3)
C22A—C23A	1.378 (3)	C22B—C23B	1.371 (3)
C23A—C24A	1.370 (3)	C23B—C24B	1.369 (4)
C24A—C25A	1.369 (3)	C24B—C25B	1.363 (4)
C25A—C26A	1.383 (3)	C25B—C26B	1.387 (4)
N6A—O62A	1.216 (3)	N6B—O62B	1.209 (3)
N6A—O61A	1.222 (3)	N6B—O61B	1.223 (3)
C8AA—N1A—C2A	119.98 (19)	C8AB—N1B—C2B	119.90 (19)
C8AA—N1A—C1A	119.22 (19)	C8AB—N1B—C1B	118.95 (19)

C2A—N1A—C1A	119.83 (19)	C2B—N1B—C1B	121.01 (19)
C3A—C2A—N1A	122.8 (2)	C3B—C2B—N1B	122.6 (2)
C3A—C2A—C21A	120.4 (2)	C3B—C2B—C21B	120.2 (2)
N1A—C2A—C21A	116.72 (19)	N1B—C2B—C21B	117.2 (2)
C2A—C3A—C4A	120.4 (2)	C2B—C3B—C4B	120.8 (2)
C2A—C3A—C31A	122.4 (2)	C2B—C3B—C31B	122.7 (2)
C4A—C3A—C31A	117.2 (2)	C4B—C3B—C31B	116.5 (2)
O4A—C4A—C3A	122.8 (2)	O4B—C4B—C3B	123.9 (2)
O4A—C4A—C4AA	121.3 (2)	O4B—C4B—C4AB	120.8 (2)
C3A—C4A—C4AA	115.9 (2)	C3B—C4B—C4AB	115.4 (2)
C5A—C4AA—C8AA	119.6 (2)	C5B—C4AB—C8AB	119.5 (2)
C5A—C4AA—C4A	119.4 (2)	C5B—C4AB—C4B	119.2 (2)
C8AA—C4AA—C4A	121.0 (2)	C8AB—C4AB—C4B	121.3 (2)
C6A—C5A—C4AA	119.8 (2)	C6B—C5B—C4AB	119.5 (2)
C5A—C6A—C7A	121.6 (2)	C5B—C6B—C7B	122.2 (2)
C5A—C6A—N6A	119.3 (3)	C5B—C6B—N6B	118.9 (2)
C7A—C6A—N6A	119.0 (2)	C7B—C6B—N6B	118.9 (2)
C8A—C7A—C6A	119.2 (2)	C8B—C7B—C6B	118.9 (2)
C7A—C8A—C8AA	120.4 (2)	C7B—C8B—C8AB	120.7 (2)
N1A—C8AA—C8A	121.2 (2)	N1B—C8AB—C4AB	119.6 (2)
N1A—C8AA—C4AA	119.4 (2)	N1B—C8AB—C8B	121.3 (2)
C8A—C8AA—C4AA	119.4 (2)	C4AB—C8AB—C8B	119.1 (2)
N1A—C1A—C11A	116.84 (18)	N1B—C1B—C11B	115.38 (18)
C16A—C11A—C12A	118.6 (2)	C12B—C11B—C16B	118.7 (2)
C16A—C11A—C1A	123.9 (2)	C12B—C11B—C1B	122.7 (2)
C12A—C11A—C1A	117.5 (2)	C16B—C11B—C1B	118.6 (2)
C13A—C12A—C11A	120.2 (3)	C11B—C12B—C13B	120.2 (2)
C14A—C13A—C12A	120.6 (3)	C14B—C13B—C12B	120.8 (3)
C13A—C14A—C15A	119.2 (3)	C13B—C14B—C15B	119.1 (3)
C14A—C15A—C16A	120.7 (3)	C14B—C15B—C16B	120.6 (3)
C11A—C16A—C15A	120.6 (3)	C15B—C16B—C11B	120.6 (3)
C22A—C21A—C26A	119.6 (2)	C26B—C21B—C22B	118.9 (2)
C22A—C21A—C2A	118.9 (2)	C26B—C21B—C2B	120.0 (2)
C26A—C21A—C2A	121.4 (2)	C22B—C21B—C2B	121.0 (2)
C21A—C22A—C23A	120.1 (2)	C23B—C22B—C21B	120.5 (3)
C24A—C23A—C22A	120.3 (2)	C24B—C23B—C22B	120.0 (3)
C25A—C24A—C23A	120.1 (2)	C25B—C24B—C23B	120.7 (3)

C24A—C25A—C26A	120.2 (2)	C24B—C25B—C26B	119.7 (3)
C25A—C26A—C21A	119.8 (2)	C21B—C26B—C25B	120.2 (3)
O62A—N6A—O61A	122.9 (3)	O62B—N6B—O61B	123.7 (3)
O62A—N6A—C6A	118.5 (3)	O62B—N6B—C6B	118.1 (3)
O61A—N6A—C6A	118.6 (3)	O61B—N6B—C6B	118.2 (3)
C8AA—N1A—C2A—C3A	6.9 (3)	C8AB—N1B—C2B—C3B	-5.4 (3)
C1A—N1A—C2A—C3A	-161.7 (2)	C1B—N1B—C2B—C3B	170.2 (2)
C8AA—N1A—C2A—C21A	-170.47 (18)	C8AB—N1B—C2B—C21B	173.81 (19)
C1A—N1A—C2A—C21A	20.9 (3)	C1B—N1B—C2B—C21B	-10.6 (3)
N1A—C2A—C3A—C4A	-1.0 (3)	N1B—C2B—C3B—C4B	0.2 (3)
C21A—C2A—C3A—C4A	176.34 (19)	C21B—C2B—C3B—C4B	-178.95 (19)
N1A—C2A—C3A—C31A	179.6 (2)	N1B—C2B—C3B—C31B	-180.0 (2)
C21A—C2A—C3A—C31A	-3.1 (3)	C21B—C2B—C3B—C31B	0.8 (3)
C2A—C3A—C4A—O4A	176.5 (2)	C2B—C3B—C4B—O4B	-175.9 (2)
C31A—C3A—C4A—O4A	-4.1 (3)	C31B—C3B—C4B—O4B	4.3 (3)
C2A—C3A—C4A—C4AA	-4.9 (3)	C2B—C3B—C4B—C4AB	4.7 (3)
C31A—C3A—C4A—C4AA	174.53 (19)	C31B—C3B—C4B—C4AB	-175.14 (19)
O4A—C4A—C4AA—C5A	3.9 (3)	O4B—C4B—C4AB—C5B	-4.3 (3)
C3A—C4A—C4AA—C5A	-174.75 (18)	C3B—C4B—C4AB—C5B	175.19 (18)
O4A—C4A—C4AA—C8AA	-176.1 (2)	O4B—C4B—C4AB—C8AB	175.7 (2)
C3A—C4A—C4AA—C8AA	5.2 (3)	C3B—C4B—C4AB—C8AB	-4.8 (3)
C8AA—C4AA—C5A—C6A	-0.8 (3)	C8AB—C4AB—C5B—C6B	0.1 (3)
C4A—C4AA—C5A—C6A	179.22 (19)	C4B—C4AB—C5B—C6B	-179.87 (19)
C4AA—C5A—C6A—	0.3 (3)	C4AB—C5B—C6B—	-0.4 (3)

C7A		C7B	
C4AA—C5A—C6A—N6A	-178.65 (19)	C4AB—C5B—C6B—N6B	178.70 (19)
C5A—C6A—C7A—C8A	0.3 (3)	C5B—C6B—C7B—C8B	0.1 (3)
N6A—C6A—C7A—C8A	179.2 (2)	N6B—C6B—C7B—C8B	-179.0 (2)
C6A—C7A—C8A—C8AA	-0.3 (3)	C6B—C7B—C8B—C8AB	0.4 (3)
C2A—N1A—C8AA—C8A	173.13 (19)	C2B—N1B—C8AB—C4AB	5.1 (3)
C1A—N1A—C8AA—C8A	-18.1 (3)	C1B—N1B—C8AB—C4AB	-170.59 (18)
C2A—N1A—C8AA—C4AA	-6.4 (3)	C2B—N1B—C8AB—C8B	-175.23 (19)
C1A—N1A—C8AA—C4AA	162.32 (18)	C1B—N1B—C8AB—C8B	9.1 (3)
C7A—C8A—C8AA—N1A	-179.8 (2)	C5B—C4AB—C8AB—N1B	-179.97 (18)
C7A—C8A—C8AA—C4AA	-0.2 (3)	C4B—C4AB—C8AB—N1B	0.0 (3)
C5A—C4AA—C8AA—N1A	-179.71 (18)	C5B—C4AB—C8AB—C8B	0.4 (3)
C4A—C4AA—C8AA—N1A	0.3 (3)	C4B—C4AB—C8AB—C8B	-179.63 (19)
C5A—C4AA—C8AA—C8A	0.8 (3)	C7B—C8B—C8AB—N1B	179.7 (2)
C4A—C4AA—C8AA—C8A	-179.24 (18)	C7B—C8B—C8AB—C4AB	-0.7 (3)
C8AA—N1A—C1A—C11A	85.1 (2)	C8AB—N1B—C1B—C11B	-75.8 (3)
C2A—N1A—C1A—C11A	-106.2 (2)	C2B—N1B—C1B—C11B	108.5 (2)
N1A—C1A—C11A—C16A	1.3 (3)	N1B—C1B—C11B—C12B	-25.3 (3)
N1A—C1A—C11A—C12A	-177.8 (2)	N1B—C1B—C11B—C16B	157.4 (2)
C16A—C11A—C12A—C13A	-0.7 (4)	C16B—C11B—C12B—C13B	0.6 (4)
C1A—C11A—C12A—C13A	178.5 (2)	C1B—C11B—C12B—C13B	-176.7 (2)
C11A—C12A—C13A—C14A	-1.3 (4)	C11B—C12B—C13B—C14B	-1.1 (4)
C12A—C13A—C14A—C15A	1.7 (5)	C12B—C13B—C14B—C15B	1.1 (4)

C13A—C14A—C15A—C16A	-0.2 (5)	C13B—C14B—C15B—C16B	-0.6 (5)
C12A—C11A—C16A—C15A	2.1 (4)	C14B—C15B—C16B—C11B	0.1 (4)
C1A—C11A—C16A—C15A	-177.0 (2)	C12B—C11B—C16B—C15B	-0.1 (4)
C14A—C15A—C16A—C11A	-1.7 (4)	C1B—C11B—C16B—C15B	177.3 (2)
C3A—C2A—C21A—C22A	-97.7 (3)	C3B—C2B—C21B—C26B	89.7 (3)
N1A—C2A—C21A—C22A	79.8 (3)	N1B—C2B—C21B—C26B	-89.5 (3)
C3A—C2A—C21A—C26A	78.5 (3)	C3B—C2B—C21B—C22B	-86.8 (3)
N1A—C2A—C21A—C26A	-104.0 (2)	N1B—C2B—C21B—C22B	94.0 (3)
C26A—C21A—C22A—C23A	0.4 (4)	C26B—C21B—C22B—C23B	0.4 (4)
C2A—C21A—C22A—C23A	176.7 (2)	C2B—C21B—C22B—C23B	176.9 (2)
C21A—C22A—C23A—C24A	0.1 (4)	C21B—C22B—C23B—C24B	-1.1 (4)
C22A—C23A—C24A—C25A	-0.5 (4)	C22B—C23B—C24B—C25B	1.6 (4)
C23A—C24A—C25A—C26A	0.5 (4)	C23B—C24B—C25B—C26B	-1.4 (4)
C24A—C25A—C26A—C21A	0.0 (4)	C22B—C21B—C26B—C25B	-0.1 (4)
C22A—C21A—C26A—C25A	-0.5 (3)	C2B—C21B—C26B—C25B	-176.7 (2)
C2A—C21A—C26A—C25A	-176.7 (2)	C24B—C25B—C26B—C21B	0.6 (4)
C5A—C6A—N6A—O62A	-174.9 (2)	C5B—C6B—N6B—O62B	-176.0 (2)
C7A—C6A—N6A—O62A	6.1 (3)	C7B—C6B—N6B—O62B	3.1 (3)
C5A—C6A—N6A—O61A	6.3 (3)	C5B—C6B—N6B—O61B	0.9 (3)
C7A—C6A—N6A—O61A	-172.7 (2)	C7B—C6B—N6B—O61B	180.0 (2)



VITA

James Ervin Schammerhorn III

Candidate for the Degree of

Doctor of Philosophy

Thesis: NEW TANDEM REACTIONS INVOLVING NUCLEOPHILIC AROMATIC SUBSTITUTION

Major Field: Chemistry

Biographical:

Personal Data: Born in Oklahoma City, Oklahoma, to James and Glenda Schammerhorn, Citizenship: USA

Education: Completed the requirements for the Associates of Science at Murray State College, Tishomingo, Oklahoma in May, 2003 (CRC award for Outstanding Freshman Chemistry Student); Completed the requirements for the Bachelor of Science in Chemistry at Oklahoma State University, Stillwater, Oklahoma in May, 2006 (Outstanding Graduating Chemistry Senior).

Experience: Graduate Teaching Assistant, Dept. of Chemistry, OSU, Fall, 2006-present; Teaching Assistant, Dept. of Chemistry, OSU, Fall, 2005-Spring 2006; Storeroom Attendant, Dept. of Chemistry, OSU, Fall, 2003-Fall 2004; Chemistry Storeroom Attendant, Murray State College, Fall, 2001-Spring 2003

Professional Memberships: American Chemical Society, Phi Lambda Upsilon Chemistry Honor Society, Golden Key Honor Society, Phi Theta Kappa Honor Society

Name: James Ervin Schammerhorn III Date of Degree: May, 2011

Institution: Oklahoma State University Location: Stillwater, Oklahoma

Title of Study: NEW TANDEM REACTIONS INVOLVING NUCLEOPHILIC AROMATIC SUBSTITUTION

Pages in Study: 123 Candidate for the Degree of Doctor of Philosophy

Major Field: Chemistry

Scope and Method of Study: The synthesis of 6-nitro-1,2,3,4-tetrahydroquinoline-4-carboxylic esters and 7-nitro-3,4-dihydroquinoxaline-1(2*H*)-carboxylic esters employing a tandem reductive amination-S_NAr reaction is described. In addition, a tandem imine addition-S_NAr reaction allowing the preparation of highly substituted 1,2,3,4-tetrahydroquinolines is also reported.

Findings and Conclusions: The development of a new route to nitro-substituted tetrahydroquinoline-4- carboxylic esters and dihydroquinoxaline-1(2*H*)-carboxylic esters is based on a tandem reductive amination-S_NAr reaction. In this sequence, an electron deficient aromatic ring is critical to the final S_NAr ring closure. The reaction is also sensitive to steric hindrance in the amine, with primary amines giving the highest yields. Though the current approach to the tetrahydroquinoline systems is not as diastereoselective as our earlier-reported reduction-reductive amination, it does offer a relatively direct route to the title compounds.

The development of a tandem imine addition-S_NAr annulation reaction has afforded a new approach to 1,2,3,4-tetrahydroquinolinone-3-carboxylate esters. A series of 1-alkyl-2-aryl-6-nitro-4-oxo-1,2,3,4-tetrahydroquinolinone-3-carboxylate esters have been generated by reacting an imine with a β-ketoester substituted at C3 by a 2-fluoro-5-nitrophenyl group. Variation in the final product is possible through changes in the structure of the imine and potentially by altering the electron-withdrawing group on the aromatic acceptor. The imines are formed by reacting a 1:1.2 ratio of a primary amine unbranched α to the nitrogen with an aldehyde derivative in *N*,*N*-dimethylformamide for 6 hours. The β-ketoester is then added to initiate a spontaneous tandem reaction to produce the substituted 1,2,3,4-tetrahydroquinolinone-3-carboxylate esters in 73-89% yields. The reaction occurs without the need for added base or heat. Future work will include determining conditions that can support the use of other imines to broaden the scope of the process.

ADVISER'S APPROVAL: Dr. Richard A. Bunce